THE American Journal OF Gastroenterology

VOL. 27, NO. 6 JUNE, 1957

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Boston, Massachusetts
20, 21, 22, 23 October 1957

Official Publication
AMERICAN COLLEGE
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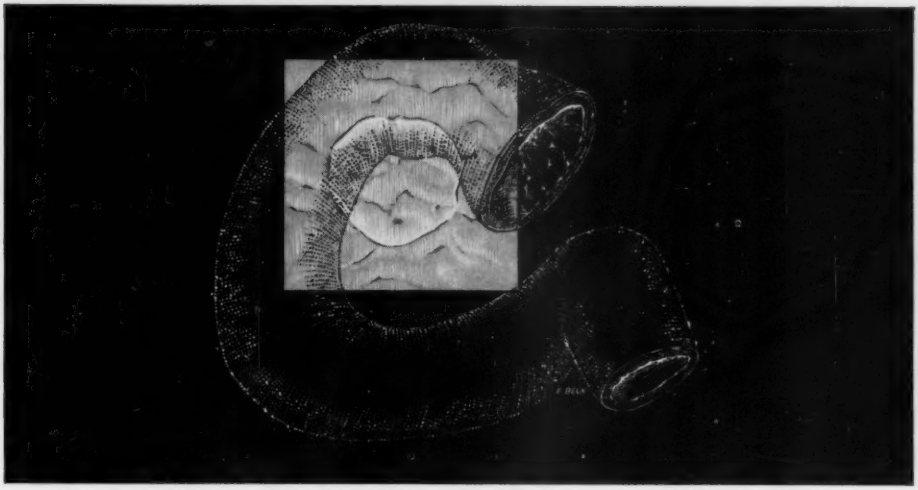

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VOL. 27, No. 6 JUNE, 1957

THE American Journal OF Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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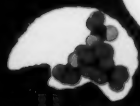

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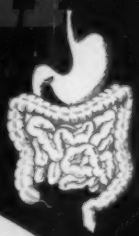

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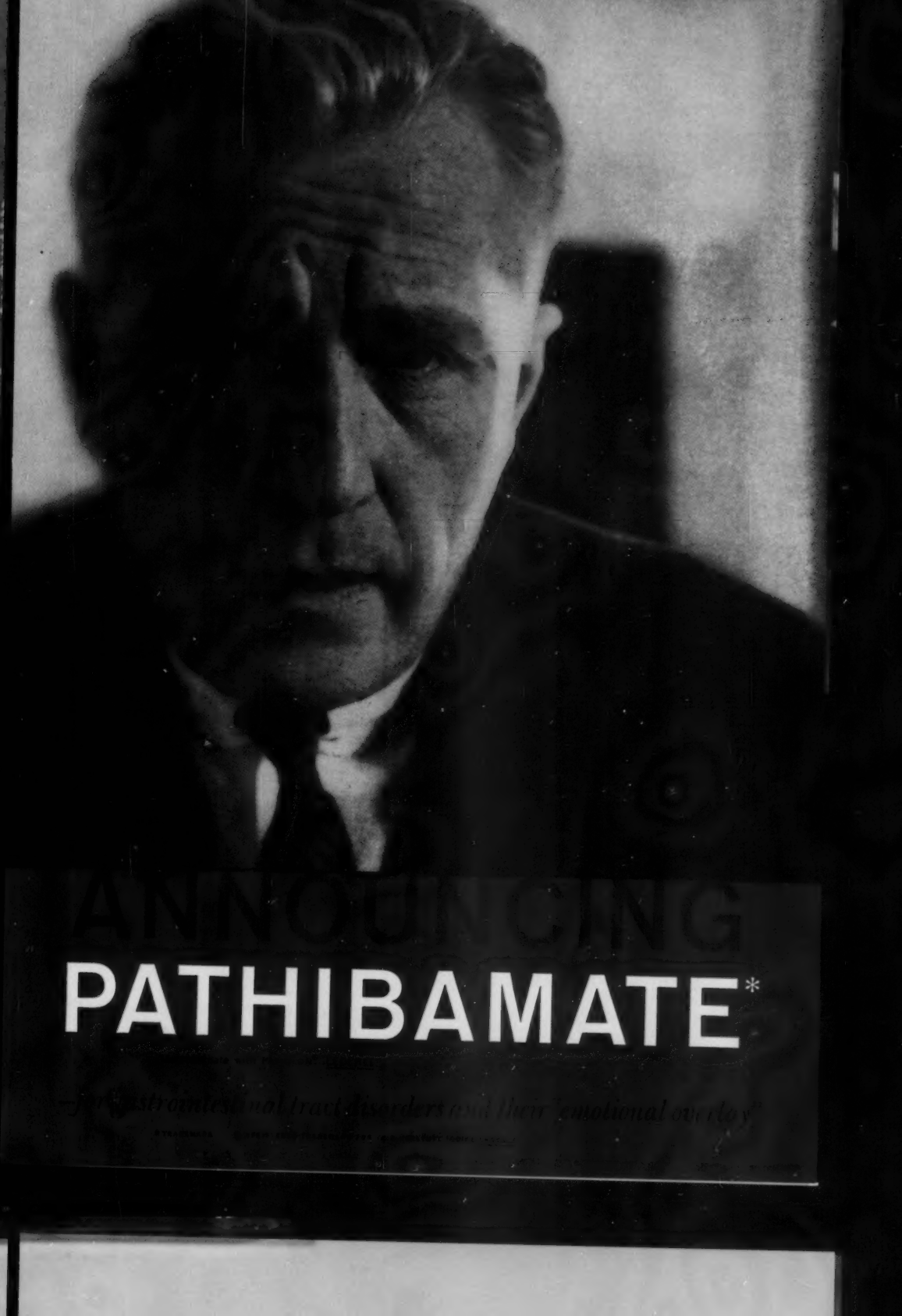
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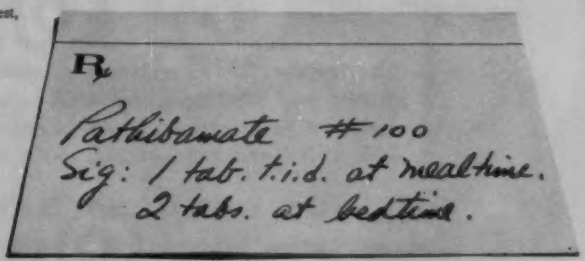

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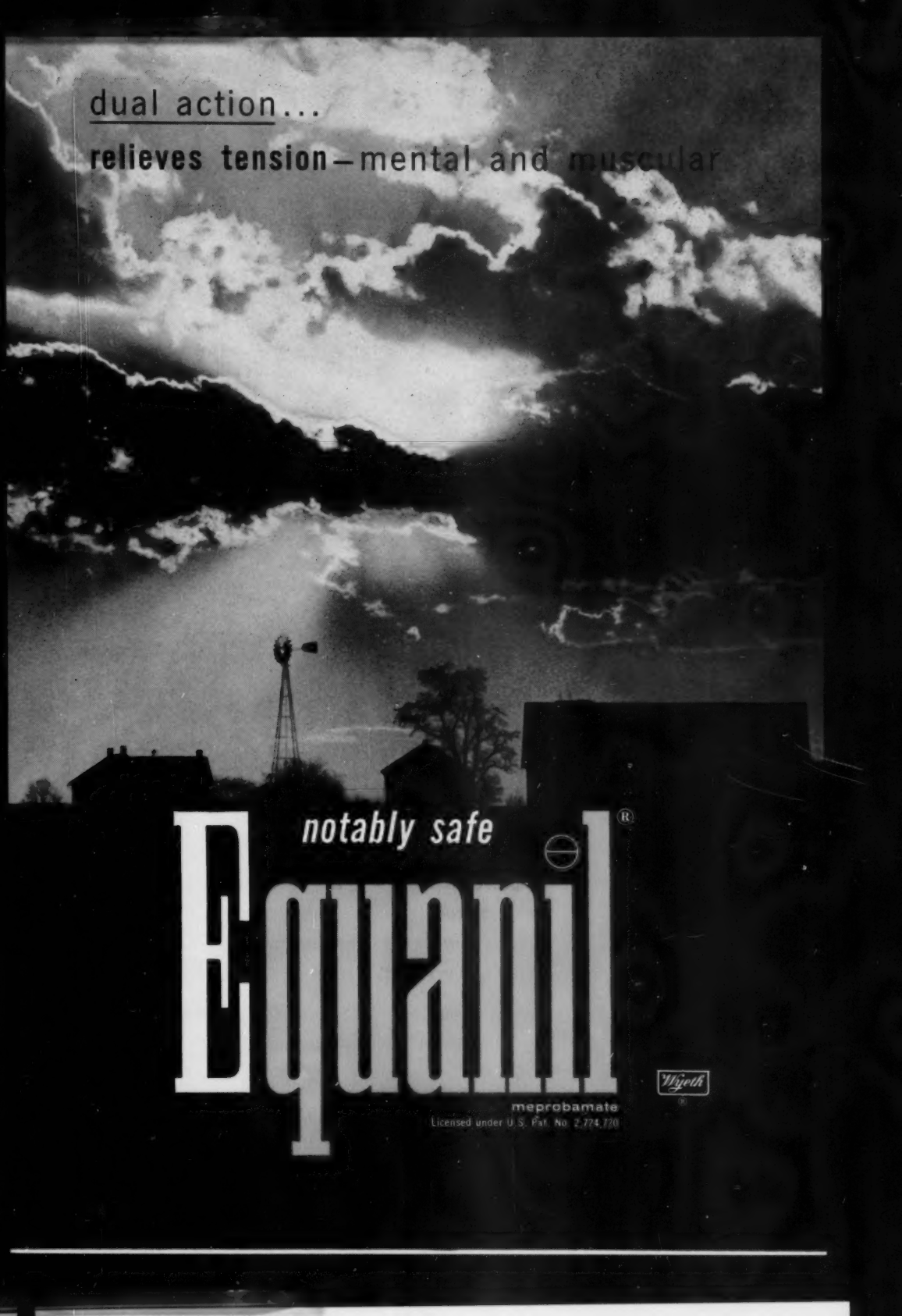
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THE American Journal OF Gastroenterology

A monthly journal of Gastroenterology, Proctology and Allied Subjects
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VOLUME 27 JUNE, 1957 NUMBER 6

THE MANAGEMENT OF CHRONIC NONSPECIFIC DIARRHEA

GASTROENTEROLOGICAL CLINICAL CONFERENCE*

HARRY BAROWSKY, B.S., M.D., F.A.C.G., Chairman†
GEORGE B. JERZY GLASS, M.D., F.A.C.P., F.A.C.G.‡
STANLEY H. CRAIG, M.D., F.A.C.G.¶
NATHAN W. CHAIKIN, B.S., M.D., F.A.C.P., F.A.C.G.§
CHARLES L. FOX, JR., M.D.♯
SAUL A. SCHWARTZ, M.D., F.A.C.G.**
MARCEL E. MARTINEZ, M.D.††
New York, N. Y.
I. SNAPPER, M.D., Ph.D., F.A.C.G. (Hon.)‡‡
Brooklyn, N. Y.
and
OWEN H. WANGENSTEEN, B.A., M.D., Ph.D.¶¶
Minneapolis, Minn.

Dr. Harry Barowsky:—On behalf of the New York Medical College, I want to extend a cordial welcome to those taking the Postgraduate Course of the American College of Gastroenterology.

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*Presented at the Metropolitan Medical Center, New York, N. Y., as part of the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, New York, N. Y., 18, 19, 20 October 1956.

†Assistant Professor of Medicine, New York Medical College; Associate in Medicine, Flower and Fifth Avenue Hospitals, Metropolitan Medical Center and Bird S. Coler Hospital; Consultant Gastroenterologist to Prospect Heights Hospital.

‡Associate Professor of Medicine, New York Medical College.

¶Assistant Clinical Professor of Radiology, New York Medical College.

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**Assistant Clinical Professor of Medicine, New York Medical College.

††Fellow in Gastroenterology, Metropolitan Medical Center.

‡‡Director, Department of Medicine, Beth-El Hospital.

¶¶Professor and Chairman, Department of Surgery, University of Minnesota School of Medicine.

Those participating in this conference are:

Dr. George B. Jerzy Glass, Associate Professor of Medicine and Director of the Gastroenterology Research Laboratory, New York Medical College, Flower and Fifth Avenue Hospitals and Metropolitan Medical Center;

Dr. Stanley H. Craig, Assistant Clinical Professor of Radiology, New York Medical College, Flower and Fifth Avenue Hospital and Metropolitan Medical Center;

Dr. Nathan W. Chaikin, Associate Clinical Professor of Medicine, New York Medical College, Flower and Fifth Avenue Hospital; Attending, Metropolitan Medical Center, Bird S. Coler Hospital;

Dr. Charles L. Fox, Jr., Associate Professor of Surgery, New York Medical College, Flower and Fifth Avenue Hospital and Metropolitan Medical Center;

Dr. Saul A. Schwartz, Assistant Clinical Professor of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals; Associate in Medicine, Division Gastroenterology, Metropolitan Medical Center and Bird S. Coler Hospital and

Dr. Marcial E. Martinez, Fellow in Gastroenterology, Metropolitan Medical Center.

Also participating are our Course moderators: Dr. I. Snapper, Director of the Department of Medicine at the Beth-El Hospital, Brooklyn, N. Y. and

Dr. Owen H. Wangensteen, Director of the Department of Surgery, University of Minnesota School of Medicine, Minneapolis, Minn.

The subject of this Clinical Conference will be the Management of Chronic Nonspecific Diarrhea. Conditions included in this category will be ulcerative colitis, regional enteritis and other allied disturbances causing protracted diarrhea but where the etiology has not been established. The management of this type of disturbance presents a complex of therapeutic problems. I would like to ask the members of the panel to amplify in their discussion the therapeutic aspects of the measures employed in: 1. Suppressing the diarrhea. 2. Maintaining nutrition and restoring blood loss. 3. Controlling secondary infection. 4. Steroid therapy. 5. Surgical procedures and 6. The correction of water and electrolyte balance.

I will now ask Dr. Schwartz to read to us the history of the first case.

Dr. Saul A. Schwartz:—G. K., a 26-year old white male, entered Metropolitan Hospital on 5 July 1956, referred by a L.M.D. with the chief complaints of:

1. Swelling of legs, ankle and abdomen, for 2 months.

2. Diarrhea 6 to 8 B.M.'s daily, of 5 years' duration.

3. Shortness of breath of 2 months' duration.

Present Illness:–In June 1951 the patient complained of frequent B.M.'s, with occasional mucus and blood in the stools. The B.M.'s were preceded by abdominal cramps. In November he was hospitalized for these symptoms in another institution. Studies at that time revealed an extensive ulcerative colitis. The treatment with high caloric diet, bismuth, kaolin, paregoric, high doses of multivitamins by injection, and ACTH, controlled his symptoms and he was discharged.

One month later he had a relapse, having 6 to 8 B.M.'s a day, which continued for 2 years, and in spite of rehospitalization and administration of the same measures, no improvement occurred.

In the spring of 1955 the patient suddenly developed a disturbance of his equilibrium and coordination of the use of his arms and legs. He was admitted to the Neurological Institute and a diagnosis of demyelinizing process, such as encephalomyelitis or multiple sclerosis was made and he improved under observation.

In April 1956, during routine examination by his physician, a massive albuminuria was found. The patient had gained 10 lbs. He was hospitalized about 1 week later. His blood pressure rose from 120/85 to 155/105. The urine sediment showed RBC's, WBC's, and a good number of hyalin and granular casts. The blood urea nitrogen rose from a normal of 13 to 48 mg. per cent. Total serum proteins 7.3 gm. per cent. Albumin 3.5 gm. per cent, globulin 3.8 gm. per cent. The electrolytes were within normal limits at first, but later sodium was 127 mEq/l. and potassium went up to 6.5 mEq/l.

At the hospital he was treated with 2,000 c.c. of fluid intake daily, cortisone 300 mg. qd. for a period of 1 week, 200 mg. qd. for the following 2 weeks, 100 mg. qd. for another 2 weeks, and then 50 mg. qd. for another 2 weeks; ammonium chloride orally and infusion of 5 per cent dextrose in water mixed with salt poor human albumin, and salt free diet. The clinical picture improved remarkably under this therapy. The blood urea nitrogen became normal, the edema disappeared, the blood pressure fell to 130/90 and the patient regained his appetite. He was discharged in May 1956.

In spite of continuation of the same dietary regime, rest and medication, his condition deteriorated again. The edema of his legs, ankles and abdomen reappeared and he developed shortness of breath, anorexia, and 6 to 8 B.M.'s daily, watery and loose in consistency. He was readmitted to Metropolitan Hospital on 5 July 1956.

Past History:–Measles and chickenpox in childhood.

Family History:–Not contributory.

Physical Examination:—EENT, negative. Cardiovascular, negative. Lungs, negative. Abdomen, soft on palpation. Liver, spleen and masses not palpable. Shifting dullness and fluid waves were present. Barium enema and sigmoidoscopy were characteristic of ulcerative colitis.

Laboratory data on admission:—RBC 4,300,000, WBC 6,600, Hb. 13.9 gm. Hematocrit 48. Seg. 60 per cent, Staph., 5 per cent, Lymph 35 per cent. *Blood Chemistry:*—Total serum protein 3.3 gm. per cent, albumin 0.9 gm. per cent, globulin 2.4 gm. per cent, cholesterol 670 mg. per cent esters, total 482 mg. per cent, glucose 115 mg. per cent, blood urea nitrogen 34 mg. per cent, Na 130.6 mEq/l. K 5.7 mEq/l. chlorides 120 mEq/l. CO_2 combining power 38 vol. per cent, *Urinalysis:*—Color yellow. Appearance, cloudy; pH 4.5, Sp. Gr. 1.025. Albumin 4+, WBC 8 to 10 per high power field. Crystals amorphous.

Treatment at the hospital included:—1. Salt free diet. 2. High protein diet. 3. ACTH 50 units intramuscularly q.6.h. for 22 days, then cortisone 100 mg. q.6.h. for 3 successive days each week, for 3 weeks. 4. Paregoric drams 1 after each B.M. 5. Potassium chloride gr. xv t.i.d. After three weeks of therapy the B.M.'s diminished to 4 a day, and were soft in consistency. His appetite improved and the anasarca subsided. The patient was discharged on 23 August 1956 for follow-up at the clinic. Present treatment consists of cortisone 100 mg q.6.h. for three successive days each week and regular diet. At present he feels well, and has 2 well-formed B.M.'s daily.

Last urinalysis at the clinic 25 September 1956: color, yellow; appearance clear. Sp.Gr. 1.016, albumin 1+ to 2+. WBC occasional. Cast—modified hyaline. Blood pressure 130/90.

Dr. Barowsky:—Thank you, Dr. Schwartz.

So far, from the clinical history, we have a classic example of a protracted case of ulcerative colitis except for some complications of a neurological nature and a nephritis or a nephrotic syndrome which this patient later developed. I will ask the panel to exclude these complications from their discussion, unless time permits us to take them up.

Dr. Craig will now show us the x-ray films of this case.

Dr. Stanley H. Craig:—The first series that you see on top show the colon before treatment; in other words, the patient, I believe, was admitted on the 5th or the 8th, one of those days, and these were taken on the 11th of July. You notice we are dealing with a rather narrow colon which appears somewhat shortened. The haustral markings are completely gone and there are variations present throughout the colon. One must conclude this is a typical case of ulcerative colitis of long standing. The only thing I do not see very well on the film is the persistent narrow areas in the colon, we sometimes see, in a long standing case of ulcerative colitis.

Following the treatment, you will notice that the colon assumed a normal size; however, the haustral markings are still absent. I must say following the treatment it looks considerably better than on the original films, but we cannot call this a normal colon.

Dr. Barowsky:—Dr. Craig, what happened to the marked narrowing and stiffening of the colon seen in the early x-ray films? How do you explain the fact that the colon now looks more normal roentgenographically? Our impression is that this is a chronic advanced case with marked granulomatous inflammation and fibrosis, and we would not expect to see too much improvement at this stage. This man has had active ulcerative colitis since 1951.

Dr. Craig:—I think we are dealing more with a local spasm in the colon series, instead of advanced fibrosis, because if it were straight fibrosis, I doubt whether you would get a balloon outline. There was considerable spasm in the first series taken. I don't doubt but that there is some fibrosis present.

Dr. Barowsky:—I will now have the patient come in, so the members of the panel may ask him some questions.

Dr. O. H. Wangensteen:—Was this patient proctoscopically negative?

Dr. Barowsky:—No, he wasn't. We found characteristic proctoscopic findings of a diffusely inflamed mucous membrane.

Here is the patient. Are there any questions the panel would like to ask him?

Dr. I. Snapper:—Has he been in the army?

Patient:—No.

Dr. Wangensteen:—Has he had tropical experience?

Patient:—No.

Dr. Snapper:—Florida?

Patient:—Just New York and Pennsylvania.

Dr. Wangensteen:—Do you have diarrhea now?

Patient:—No.

Dr. Wangensteen:—How many bowel movements in a day?

Patient:—Two or three.

Dr. Wangensteen:—Four or five sometimes?

Patient:—No.

Dr. Barowsky:—The last sentence in the history: "At present he feels well, and has two well-formed B.M.'s daily."

Do you feel well enough to go to work?

Patient:—I think I would wait another four weeks or so.

Dr. Wangensteen:—Do you do everything you would normally?

Patient:—Yes.

Dr. Wangensteen:—You are not in any way inhibited?

Patient:—No, I am taking it easy.

Dr. Craig:—How much weight have you gained since you left the hospital?

Patient:—About 15 pounds.

Dr. Schwartz:—He might inform the audience whether he has had any sore throats or respiratory infection before the onset of his kidney difficulty.

Patient:—No.

Dr. Barowsky:—Thank you very much. (Exit patient.)

Although we obtained an excellent result, the management of this case is standard and no different from the therapy carried out in most institutions.

There are, however, various phases of the treatment which we would like to explore more fully.

First I will ask Dr. Snapper what is the mechanism of disturbed motility in diarrhea, and what measures would he take to suppress the diarrhea. I believe this is one of the most annoying problems that confronts the doctor and it takes all his ingenuity at times to solve it.

Dr. Snapper:—The intestinal wall has to be considered as a sewer, which should not permit many of the toxic substances present in the lumen of the colon to be absorbed. As soon as widespread ulceration is present, many of the poisons which abound in the normal colon may reach the circulation. In other words, patients with ulcerative colitis are sick because substances as phenol and other toxic compounds are absorbed. The major cause of diarrhea in ulcerative colitis is the tremendous exudation of fluid which originates from the inflamed intestinal wall.

The future of a patient with ulcerative colitis depends upon his general condition: if one can improve the general condition, the ulcerative colitis will improve. Therefore we are nowadays still dependent on blood transfusions, vitamins, etc., from which the general condition benefits. Corticosteroids *may* do the same and therefore may help in certain cases, but, as you know, corticosteroids are double-edged swords and may give rise to perforations. We have no medicaments which act upon the diarrhea itself unless the drugs influence the inflammation.

Dr. Barowsky:—We will discuss that a little later, pardon me, but I merely would like you to name some of the medications doctors would like to use, and maybe you could give them some of your secrets.

Dr. Snapper:—Since one will try, if possible, to avoid habit forming drugs, like opium, in ulcerative colitis, we have to rely heavily upon adsorbent drugs, charcoal, kaolin and bismuth preparations. Often I use all three adsorbent drugs at the same time for the treatment of this disease.

Of the bismuth compounds I personally especially like dermatol, that is oxygallate of bismuth. A powder mixture of equal amounts of charcoal, kaolin and dermatol is prepared. The patient should take one or two tablespoons full of this powder, suspended in a glass of water, three times daily. These adsorbents are beneficial in a certain number of cases of ulcerative colitis. Whether this medication acts by covering the ulcerations with a protective layer or by adsorbing the toxic substances from the lumen, is not known.

At the same time one can try to influence the ulceration of the rectum by local treatment. Two tablespoonsful of one of the adsorbents, suspended in 200 c.c. of lukewarm water, given slowly as a retention enema, to be retained overnight, often has a soothing influence upon the rectal tenesmi.

Tannin belongs also to this group of drugs. Whether one takes tannic acid as such, or tannin conjugated with albumin, does not make too much difference.

Dr. Barowsky:—I will ask a question in reference to that later, thank you.

Dr. Glass, what is the mechanism of the causation of malnutrition, and how would you counteract it?

Dr. George B. Jerzy Glass:—To understand malnutrition of ulcerative colitis, we have to remember that the large intestine has not only a storage or propulsion ability, but that the right colon is an organ which still absorbs. It is known that 400 to 500 ml. of ileal fluid enters the cecum, but only 150 gm. of feces leaves the colon. The rest is absorbed in the cecum and the right side of the colon.

Now, what is absorbed in the colon? Water? Only water? No. Water and electrolytes; therefore, any defect in the absorption ability of the right colon such as one occurring in ulcerative colitis will cause a complex water and electrolyte disturbance.

There are several points which are important in order to understand how the malnutrition in ulcerative colitis develops, and why it develops. They are as follows: First is of course, the loss of appetite in the severely toxic patients, which contributes to malnutrition. Second, is the restricted diet on which these patients are often kept, for no obvious reasons.

The third point, more important, is the defect in the intestinal absorption. Because of it, patients lose a lot of water, and a lot of sodium. Ulcerative colitis is therefore a sodium-losing disease. The reason for that is the disturbance in the absorption ability of the right side of the colon and also a tremendous exudation of interstitial fluid into the lumen of the colon which carries large amounts of sodium with it. There is much more sodium than chloride lost in ulcerative colitis. There are also some other substances which are not properly absorbed because of the disease of the colon, such as Vitamin K. This may result in prothrombin defect. There probably also are some other vitamins which may be absorbed in the right side of the gut, and which are not absorbed adequately in this disease.

The next point, most important, is the loss of proteins in the intestinal secretion, due to excessive exudation of the intestinal fluids into the gut. This causes losses of many protein components important for our nutrition, such as serum albumin, mucus and blood. Since the interstitial fluid, which passes into intestine is especially rich in albumin, hypalbuminemia develops in these cases.

As result, all these patients develop highly negative nitrogen balance. If we calculate on one side the amount of nitrogen they take in and on the other—the amount of nitrogen they lose in the stool and urine, we find that the balance is exceedingly negative, and much more deficient than all of us realize. There are some fine studies done on the nitrogen balance in patients with ulcerative colitis, where the subjects were followed-up for several weeks after the termination of the disease. It was found that these patients remained in nitrogen deficit for many weeks after they recovered from their disease. This means that they need tremendous doses of nitrogen substances in order to be built back to their previous nitrogen status.

Dr. Barowsky:—Pardon me, Dr. Glass. Will you include in your discussion some mention of how you combat these various disturbances. We haven't too much time, and I should like to limit the discussion to dietary and therapeutic aspects.

Dr. Glass:—Because of the nitrogen deficiency, we have to supply proteins to these patients. The best way is to give high protein diet, which would include also easily digestible proteins like gelatine, egg whites, ground meat, cottage cheese, and the proteins of skim milk. Some people give protein hydrolysates, which I do not like because they increase hypermotility of the gut. The best way is to give high doses of salt free crystalline serum albumin intravenously. The loss of 1 gm. albumin per cent from serum requires the supply of about 20 gm. of albumin parenterally. On this basis we have to calculate how much albumin should be given intravenously to these patients. This treatment is, however, expensive.

The loss of vitamins should be also replaced, best by parenteral administration. The loss of electrolytes should be replaced according to the blood chem-

istry. The loss of fats usually does not occur in ulcerative colitis unless we have right-sided colitis which involves also the distal part of the ileum. In this instance there may be a loss of fat, and some people advise to administer fat suspension intravenously. The carbohydrates in general also are not lacking: they are usually included in the diet, *ad libitum*, though some sugars like fructose and lactose may increase diarrheas.

Dr. Barowsky:—Thank you, Dr. Glass.

Both previous speakers have mentioned the fact that there is a disturbance in the water and electrolyte balance. I will ask Dr. Fox to discuss the subject more extensively. I have three questions which I should like him to include in his discussion:

1. What are the clinical manifestations of disturbance of water and electrolyte balance?

2. What are the significant laboratory findings?

3. How would you adjust these disturbances?

Dr. Fox!

Dr. Charles L. Fox:—Some of the electrolyte problems that are involved here vary tremendously from case to case, and I think it would be very difficult to generalize; however, with the present patient, I think there are certain indications of the nature of the problem.

It is important to recognize or to emphasize, as mentioned by Dr. Snapper and Dr. Glass, that the gastrointestinal fluids contain large amounts of electrolytes and water. Specifically these patients lose large amounts of sodium, more sodium than chloride, and large amounts of potassium.

These losses cause certain disturbances. With the loss of body fluid, there is a diminution of blood volume, and, with the diminution of blood volume, there will be some failure of renal function, as seen in this patient in the rising blood urea nitrogen. The mild hypertension is difficult to explain. In addition, the patient shows a moderate degree of acidosis. The CO_2 combining power is 38 volumes per cent, which is subnormal, and chlorides are elevated, indicating the larger loss of sodium, and the tendency of chloride to be above normal and bicarbonate below normal.

We may find some obvious manifestations of acidosis in terms of increased depth of respiration. It isn't mentioned whether the man's respiratory function was altered.

Dr. Barowsky:—There was dyspnea.

Dr. Fox:—He did have dyspnea, then, which would be associated with the acidosis and with the reduction in blood volume.

Now, to confuse the situation further, there is a swelling of the legs, and ankles, and the abdomen. It is hard to explain these until one recognizes that with a protracted loss of potassium, and with a diarrhea which is causing a marked protein diminution, we know that now there is continued loss of body protein. By "loss of body protein," I do not mean only albumin from the plasma, but protein from the cells of the body. One must remember that about 98 per cent of the proteins in the body are in the cells, and as protein depletion continues, there is a tremendous loss of cell protein, and cell protoplasm, and during that time the extracellular volume increases and that is part of the picture of the edema which is present.

To summarize the clinical manifestations, there is acidosis, an increase in extracellular volume, with a swelling of the ankles, legs, and abdomen, and weakness associated with these disturbances, and also with the loss of potassium from the body.

The laboratory findings are in accord with these changes, and not grossly different than in other similar conditions. Usually it is not possible to make a differential diagnosis or gauge the extent of the changes by the electrolytic disturbances in the plasma, but the significant findings are as seen here, a reduction of plasma sodium and a reduction of plasma bicarbonate. The urine is extremely acid as the body does its best to compensate for the acidosis by forming an acid urine, with pH 4.5. If the urinalysis were done for electrolytes, one would find marked reduction of sodium in the urine, and frequently a very high potassium, because as the protein loss continues, the cells start to disintegrate, and potassium is removed from the body as the cells disintegrate. The plasma potassium may be elevated or low, depending on the degree of retention.

The retention in this man was normal. It is usually not possible to diagnose depletion of potassium from the plasma level.

If I may show a slide I have here, I think you will see this clearly.

(Slide) This is Figure 36 from Gamble's monograph (Lane Medical Lectures), which indicates the composition of the fluids lost. There is the electrolyte content of gastrointestinal secretions. In all these except the high gastric fluid, there is more sodium than chloride, and these contain bicarbonate. The potassium contents is shown as two or three times the plasma level. The potassium in diarrheal fluid, as found by Darrow, may be ten times as much as the potassium level of the plasma.

(Slide) With the depletion of protein, there are two profound changes throughout the entire body. In his study, Hegsted, in the *American Journal of Physiology*, spoke of the great increase in extracellular fluid and the great reduction in intracellular space as being partly responsible for the ascites and edema. In this slide the potassium space and protein space are depicted.

(Slide) This shows the reduction of plasma potassium concentration which occurs not only in patients with diseases of the large bowel but also with other disturbances of gastrointestinal tract function.

(Slide) Here is the postoperative situation with similar reductions of plasma potassium. Potassium deficiency frequently follows gastrointestinal disease largely due to the loss of potassium via the gastrointestinal fluids, and also to continued loss in the urine. As the illness continues the cells disintegrate and their potassium is removed continuously from the body. During the phase of therapy when one attempts to correct these disturbances, it is impossible to restore protein balance in the individual unless one repairs the potassium deficiency. To guarantee cell replacement, it is essential to administer potassium with protein. It may well be that one of the serious deficiencies of the protein hydrolysates is that they do not contain sufficient potassium to permit utilization of the protein precursor which they contain.

(Slide) With recognition of the sodium deficits which develop, the low plasma sodium often seen in patients following loss of sodium in gastrointestinal fluid, one frequently attempts to give sodium solutions to the patient. This slide (Fig. 37 from Gamble's monograph, loc. cit.) shows how administering sodium to correct a sodium loss, without simultaneously giving potassium to correct the potassium loss may both correct and make worse the electrolyte situation.

Here is a patient given 100 gm. of glucose and 1,200 c.c. of water daily. Both sodium and potassium are being lost from the body. When only sodium is given the sodium balance will become normal but the potassium loss becomes accelerated. If you give potassium and sodium together, you can attempt to normalize the situation and a much better result can be obtained.

(Slide) Figure 92 from Fox and Lasker, *S. Clin. North America* **35**:335, 1955, shows you an effort to improve repair and replacement solutions and, in summary, one should look at the black areas which are the places where potassium occurs. It is low in the plasma, high in the cells, and there is considerable in the urine. All these gastrointestinal fluids have large amounts of potassium. The body potassium appears in the urine and in the gastrointestinal fluid in this disease. In terms of replacement, ordinary saline solutions are totally inadequate. First they give no potassium; second they give as much chloride as sodium, although the fluid lost does not have as much chloride as sodium, but is like a balanced solution which contains more sodium than chloride. For this purpose both potassium and sodium lactate are recommended by Darrow. If the patient is well hydrated, a significantly high plasma potassium will not result. For maximum safety and for protracted therapy it is wise to give potassium by mouth, along with a high protein intake.

Dr. Barowsky:—How would these be administered orally if the patient were not hospitalized? If the patient is hospitalized, an infusion is given, and we

could use some of the solutions you recommend, but a good many of the patients are ambulatory. The doctor sees them in his office and in clinics. What would you recommend to doctors to use either in the form of potassium or food substances which would be high in potassium?

Dr. Fox:—The usual thing is to administer foods high in potassium, such as fruit juices and large amounts of meat. I think, however, one ought to recognize that fruit juices actually are relatively low in potassium. They just happen to contain more potassium than sodium. Milk also contains more potassium than sodium, roughly 50 per cent, but, to give away one of our secrets, one can say it is easy to prepare a palatable potassium solution by making a mixture of 100 gm. of potassium acetate, with 500 c.c. of simple syrup, made up to a liter, and flavored with syrup of lemon. This contains 1 mEq. of potassium per c.c. of solution, and a patient can take an ounce of this mixture three or four times a day and obtain from 50 to 100 mEq. of potassium daily in this feeding, along with the other foods which were mentioned.

I think it is a little unwise, in the face of the large deficits, to rely on foods as the only source of potassium, when a palatable potassium mixture can be given along with the foods.

Dr. Barowsky:—I will ask Dr. Snapper about another important factor in the management of these cases, control of secondary infections. We have used such medications as sulfonamides, antibiotics, and corticosteroids, Dr. Snapper, in your experience, what sulfonamide or antibiotic have you used to combat secondary infection?

Dr. Snapper:—In general, one should try to avoid antibiotics like aureomycin and terramycin, which themselves give rise to diarrhea. Although occasionally either of these two drugs may be helpful in the treatment of ulcerative colitis, usually the patients suffering from this disease do not react favorably, and—if anything—have more tendency than other patients to develop candida or monilia infections. In women the vagina is often involved. Thus I try to stay away from the mycins as much as possible, although I have sometimes been obliged to use them.

Sulfonamide preparations certainly have a modest place in the treatment of this condition. Prontosil, then sulfaguanidine, sulfasuxidine and sulfaphthaladine, all derivatives which are not absorbed from the normal intestine, have been tried in the course of the years. One special sulfonamide, to wit, asulfamide, or azopyrin, works as well as any of the sulfonamides. If azopyrin, or asulfamide, has no favorable influence, then in my opinion, there is no reason to use any other sulfa drug.

Dr. Fox:—What is the other name for that?

Dr. Snapper:—Asulfamide or azopyrin.

Dr. Barowsky:–Now we come to a very important aspect of management and that is steroid therapy. It is widely used. Such drugs as cortisone, hydrocortisone, Prednisone, Prednisolone and ACTH have been administered for long periods of time, for months and in many instances intermittently for several years.

I should like the panel members to discuss the subject more fully. First, I will ask Dr. Chaikin, who has some experience on our service with corticosteroids, to briefly introduce the subject.

Dr. Nathan W. Chaikin:–Because of limited time, I shall briefly summarize my personal experience with 21 cases of ulcerative colitis treated with steroids.

There is no doubt that the addition of adrenocortical steroids to the treatment of ulcerative colitis has been of great value. It is my opinion that their use preparatory to operative treatment as well as the tremendous improvement they bring about in the clinical status of the acutely and seriously ill, are real achievements.

Steroid therapy, however, should be employed with great caution. The recognition that serious complications are much more apt to occur with this therapy should compel one to use simultaneously all other measures; in other words: a properly integrated regime.

The indications for its use are:

1. In the acute, fulminating phase associated with systemic manifestations.

2. During recurrences in the chronic stage when complications are not present.

3. As a preoperative measure in patients requiring ileostomy.

4. As a long-term maintenance therapy in chronic, intractable colitis.

The dosage used depends upon the severity of the disease. I personally prefer the purified gel of ACTH and have given as high as 240 units intramuscularly and as low as 60 units, within 24 hours, tapering-off as the clinical picture improves. This is administered in conjunction with antibiotics and sulfonamides. I may add that this regime has completely eliminated ileostomy in the acute stage.

In my group of 21 cases, 13 were treated in the acute phase for the first time and with excellent results; 4 were treated for recurrences, previous therapy unknown, but results at this time were good; and 4 more were intractable. Of these, 2 were put on maintenance doses, and 2 came to surgery.

It should be realized that the steroids do not exert any appreciable effect upon the basic pathological process. In 9 of the acute cases, while the radiological and sigmoidoscopic findings were somewhat improved, the mucosa still

remained friable and bled upon the least application of pressure. Remissions varied from 3 to 14 months. In 4 others, neither the x-ray nor sigmoidoscopic findings were changed, and these patients had to be maintained on small doses of cortisone, 25 to 50 mg.

In another group of 4 patients who had recurrences without previous hormonal therapy, they showed good therapeutic results and responded well clinically. But here again, only 2 had improvements in the radiological and proctoscopic picture. Two were not affected; and I should like to add here that where patients were treated with maintenance doses, reactivation took place immediately after therapy was withdrawn.

Dr. Barowsky:—I should like you to be specific and state the exact dosage you have used.

Dr. Chaikin:—I usually use 60 units of ACTH gel every four hours depending upon the severity of the case; then decrease the dosage with clinical improvement. Where maintenance dosage was used, the dose was 25 mg. of cortisone daily.

Dr. Barowsky:—How long did you treat patients with these doses?

Dr. Chaikin:—In acute cases, the ACTH gel was used for three to four weeks; and where maintenance doses of cortisone were used, they were continued for four to six months.

Dr. Barowsky:—What are the complications in the use of steroid therapy in ulcerative colitis?

Dr. Chaikin:—The complications resulting from the use of steroid therapy include:

1. Recurrences which take place in a large number of cases when steroids are withdrawn; this occurred in five of my cases.

2. Infection: the lack of defense measures taken by an organism to localize and wall-off infecting agents at the site of entry, when the organism is hyperadrenocortical is well recognized. One patient developed tuberculosis, who had previously had negative chest films. If arrested TB exists, steroid therapy should be of short duration preparatory to operation in severe cases.

3. Perforation occurred in one case. It is interesting that the clinical picture changed from excellent response to the steroid therapy to rapid deterioration. In some cases, new longitudinal ulcer formation took place. If time permits I should like to show a few slides.

4. Adrenocortical failure after prior therapy is assuming a prominent place and represents a serious threat to operative survival. Tests designed to evaluate pituitary and adrenocortical function should be performed in all patients who

have received previous steroid therapy and are to be subjected to surgery. If the patient has received cortisone or ACTH in the past and it is recognized prior to surgery, it appears that the safest procedure is to repeat daily intravenous infusions of ACTH until a satisfactory eosinopenia is obtained, and then operate with a similar infusion taking place.

Dr. Barowsky:—Would you kindly summarize your conclusions?

Dr. Chaikin:—It is my impression that hormonal therapy does not replace any of the established medical or surgical measures but it is a powerful therapeutic agent in the following ways:

1. Promoting remission of acute symptoms such as fever and diarrhea, and when controlled, a number of cases will go on to satisfactory remissions under the usual supportive regimes.

2. Hormonal therapy is very useful as a supportive preoperative measure for patients who will require ileostomy.

3. ACTH and other supportive measures and antibiotics have largely eliminated emergency ileostomy.

Dr. Barowsky:—I should like to ask a few questions of the panel. We have heard about the uses of cortisone and hydrocortisone, and now some of the new analogues of both. We use ACTH. Dr. Snapper, what is your choice?

Dr. Snapper:—In very sick patients in whom everything has failed, one is obliged to give ACTH or cortisone.

Dr. Barowsky:—Do you use ACTH by the intramuscular or the intravenous drip method?

Dr. Snapper:—It is immaterial.

Dr. Barowsky:—You do not feel there is any difference?

Dr. Snapper:—No, I do not.

Dr. Barowsky:—Dr. Glass, do you feel there is any advantage, one over the other, in using the drip method or the parenteral intramuscular method?

Dr. Glass:—I think the intravenous ACTH is more active than the ACTH gel. One cannot accept one unit of ACTH gel as equivalent to one unit of intravenous ACTH. You can certainly use about one-half or two-thirds of the dose, if you give it intravenously. Then, there is another point: There are some long-lasting ACTH preparations which seem to me superior to the ACTH gel. The zinc-cortrophin seems to be better for acute cases than ACTH gel. It has longer action.

Dr. Barowsky:—Zinc-cortrophin?

Dr. Glass:—Yes. Zinc-cortrophin. It has an action which is as long as 48 hours, or at least about 36 hours. The same amount of zinc-cortrophin is certainly longer lasting than the same amount of ACTH gel.

Dr. Barowsky:—What is the dose?

Dr. Glass:—Similar to that of ACTH gel, i.e. 20, 40, or 60 units, every 24 or 36 hours, i.m.

Dr. Barowsky:—Dr. Fox, have you any preference?

Dr. Fox:—I should like to point out something on the rather fundamental physiological level. I think anyone indulging in therapy—

Dr. Barowsky (Interposing):—Are you talking about complications?

Dr. Fox:—No. It is extremely difficult to decide differences among drugs on a clinical level. It has taken years to obtain complete data on arsenicals and sulfonamides. We have good physiological data which are quite in disagreement with what has been said about the action of these different compounds, and I should like to put the record straight as to the physiological action of these substances about which there seems to be so much confusion.

Administration of ACTH will permit the individual to generate that quantity of adrenocortical steroid which his adrenal glands can produce. ACTH induces the adrenal glands to produce a certain output of these substances, and it is well known what that output is. If the individual, under the "stress" conditions of the disease, does not elaborate the quantity needed, it is not likely that administration of ACTH will produce anything more than those glands can yield, and if they are not yielding enough, you cannot get more.

It is also advisable to take into consideration the physiological form of the compound. It is known through isotope studies that hydrocortisone circulates in the blood and presumably carries out certain functions. I think, therefore, we are in a curious position of not using the most effective compound when we use cortisone in preference to hydrocortisone. We also know in recent years that the delta derivatives, Prednisone and Prednisolone have been known to be far more effective than cortisone or hydrocortisone. Prednisone is a delta dehydro derivative of cortisone and Prednisolone is the delta dehydro derivative of hydrocortisone. Prednisone and Prednisolone have been found experimentally to be three to five times more effective than hydrocortisone, and also have several advantages. They do not cause the degree of sodium retention or potassium loss associated with ACTH or cortisone, in a situation such as a nephrotic syndrome or heart disease, where one is faced with sodium retention.

It would seem wise to accept progress and start using the more effective compounds first.

Dr. Snapper:—It takes 25 years before one knows the actions and especially the side actions of a drug. Therefore, although we must certainly pay careful attention to the remarks of Dr. Fox, only the future will decide whether these physiological data are correct.

So far as the corticosteroids are concerned, we have to consider that they also influence the functions of the intestine itself. They, for instance, retard the absorption of calcium from the intestine and there is even reason to believe that in this respect differences exist between different corticosteroids.

Dr. Barowsky:—We will now discuss the surgical aspects of the problem, but before we do that, Dr. Martinez will read the history of this extremely interesting case.

Dr. Marcial E. Martinez:—S. V., a 61-year old white female entered Metropolitan Hospital on September 4, 1956, with the following chief complaints:

1. Watery diarrhea every 15 minutes, from a permanent ileostomy for one year.

2. Weakness, dizziness, for several months.

3. Itching and burning of skin around ileostomy for two months.

Present Illness:—Diarrhea from an ileostomy stoma started 1 year ago, following a total colectomy for ulcerative colitis. The diarrhea became progressively worse, and at the present it is liquid and occurs every 15 minutes. In addition she complains of weakness and dizziness. She developed some weight loss although her appetite is good; she is afraid to eat because she has a liquid bowel movement after ingestion of food. She also developed joint pain in the last few months, and complains of itching and burning of the skin around the ileostomy.

Past History:—This patient was admitted to another hospital on 8 August 1955, with the chief complaint of diarrhea, lower abdominal cramps, nausea and vomiting of several months' duration. A diagnosis of ulcerative colitis was made and a total colectomy on 26 August was performed, with permanent ileostomy.

Family History:—Not contributory.

Physical Examination:—A thin female, somewhat dehydrated and pale. Eyes, conjunctivitis right eye, and pterygium encroaching on cornea. ENT, normal. Chest, negative. Abdomen, there is a paramedian scar of the abdomen and an ileostomy in the right lower quadrant of the abdomen. A dark green watery fecal material was observed coming through the ileostomy. The peristomal skin area was markedly excoriated for about 8 cm. in diameter. Rectum, closed by suture line. Genitourinary, normal. Neurological examination, no pathological findings.

Laboratory data on admission:—RBC 3,200,000, WBC 4,600, Hb. 9 gm. Hematocrit 38, Seg. 48 per cent, Staph. 4 per cent, Lymph. 40 per cent, Eosin. 8 per cent, blood urea nitrogen 20 mg. per cent, Glucose 82 mg. per cent, Phosphorus 2.2 mg. per cent. Alk. phosphatase 7.2 units, Na. 137.2 mEq/l., K. 5.1 mEq/l., Chlorides 120 mEq/l., Cephalin flocculation 1+, Thymol turbidity 1.3 units. Total protein 6.4 gm. per cent, Albumin 3.3 gm. per cent, Globulin 3.2 gm. per cent, Gastric analysis revealed an achlorhydria.

Urinalysis:—Color yellow. Appearance—slightly cloudy, pH 7.5, Sp. Gr. 1.010, Albumin—trace. Pus cells 4-6 p.h.p.f. RBC 3-4 p.h.p.f.

Stool for ova and parasites:—negative.

Stool chemistry:—Na. 142.8 mEq/l. K. 8.7 mEq/l. Chlorides 108 mEq/l.

Urine Chemistry (24-hour):—Na.—none detectable. K. 80 mEq/l. Chlorides 80 mEq/l.

During hospital stay she developed convulsions of short duration. Blood calcium taken the following day was 6 mg. per cent. Calcium gluconate was given q.i.d. for several days.

During the hospital stay, the patient has received the following therapy:

1. Dilute HCl dram 1 in fruit juices with her meals.

2. Prolonged acting Pro-Banthine 30 mg. with her meals and before retiring.

3. Calcium gluconate.

4. Multiple vitamins.

5. Ferrous sulfate.

6. Low residue bland diet.

7. Measures were taken to prevent further excoriation of peristomal area by inserting a modified Foley catheter tube and local application of zinc ointment.

The patient improved to a marked degree. Her B.M.'s have diminished to q.r.h. and are more formed. Her skin excoriation is healing and her general condition is better.

The latest laboratory data taken revealed: RBC 4,900,000, WBC 10,900, Hb. 13.3 gm. Seg. 66, Lymph. 26 per cent, Eosin. 8 per cent, E.S.F. (Cutler) 46 per cent hematocrit.

Dr. Barowsky:—This patient, with a permanent ileostomy of one year's duration was transferred from the semi-invalidism of chronic ulcerative colitis

to being a semi-invalid with a permanent ileostomy. She has been very ill for the past year, and only on rigorous treatment which required a great deal of ingenuity, were we able to control some of her symptoms.

I will ask Dr. Wangensteen now, what are the indications for surgical intervention in these conditions?

Dr. Wangensteen:–I wish I could share the enthusiasm manifested here for protracted medical treatment of ulcerative colitis. In saying this, I am thinking of the first patient we saw. It would be good to know what his present proctoscopic findings are. We were told that at present digital examination of the rectum is negative. It is obvious from the film that he does have ulcerative colitis. There is even a possibility that he may have a cancer in the colon.

In patients treated medically and followed carefully over a period of 10 years, the incidence of observed cancer in chronic ulcerative colitis is about 10 per cent, and the over all mortality of patients treated medically for chronic ulcerative colitis over a 10-year period is approximately 50 per cent. I submit that this circumstance suggests very definitely that surgery should be invoked more often than it is in the management of chronic ulcerative colitis.

It is a little like Atlas trying to hold up the world, I think, to believe that one can juggle and hold in balance the natural constellation of the endocrines, as is being done currently in many diseases. Ultimately, the task becomes impossible and something is bound to fall out.

Recently I removed the right lobe of the liver in the course of a primary colectomy for cancer. Our only difficult problem in convalescence was occasioned by the circumstance that the patient had been given cortisone for the treatment of eczema over a long period of time. During the early convalescence, we found it necessary to give cortisone to support an adequate blood pressure. The revived administration of cortisone caused gastric hemorrhage. All in all, we had more difficulty from this iatrogenic sequence of events than from the operation. When this patient a few months hence has a "second look" operation to check on the liver, she has promised me not to take cortisone meanwhile to combat the eczema.

Having seen in our own institution how well Dr. Clarence Dennis, now of the State Medical College of New York in Brooklyn, managed patients with ulcerative colitis surgically over a period of years, I feel that surgery should be done earlier and more often than it is. I recall seeing a patient who went from our area to New York for combined medical and psychiatric treatment of chronic ulcerative colitis. After a period of some months he returned carrying a letter in his hand saying he was now 85 per cent well. That night he perforated. I saw him a few hours later and performed an ileostomy, doing a simultaneous colectomy down to the rectum. I had hoped to save the rectum with

the thought of making an ileoproctostomy later. I watched him for a period of three years, but the rectum never healed. It continued to bleed and polyps developed in the residual rectal segment, necessitating excision. As I look back now, I wish I had made a primary ileoproctostomy. My experience suggests that the intestinal current plying over a few superficial ulcers in the rectum does not harm or augment the lesion if the colon is excised.

So, if this first man whom we saw has a reasonably good rectum with only superficial ulcers and no fibrosis of the rectal wall, I would be in favor of excising 90-odd per cent of the disease, anastomosing the ileum to the mid rectum. If one sacrifices no ileum and the ileum is otherwise normal, all will be well and persistent diarrhea is unlikely. This is an operation that can be done with a very low mortality. If the cecum were healthy, I would prefer to anastomose it to the rectum.

A number of years ago (November 1940) at a meeting in the Minneapolis area, I suggested to a well-known rectal surgeon with a keen interest in ulcerative colitis, that I had anastomosed the ileum to the rectum in the management of ulcerative colitis. My friend, for such he was, looked at me with mixed feelings of surprise and pity and said: "Young man, you know nothing about ulcerative colitis." If my hair had been then as white as now, I doubt that he would have said it. For years I suffered under this criticism but gradually I learned that no one knew very much about ulcerative colitis, including my critic. Within 6 months this patient had gained 80 pounds. She has remained completely well. In 1948 Dr. Toon and I *(Am. J. Surg.* 75:384-404, 1948) reported 13 primary colectomies for fulminating ulcerative colitis, anastomosing the ileum to the rectum. When Dr. Dennis began doing vagotomy for ulcerative colitis, the problem got away from me, because his suggestion appeared to be a simpler therapeutic surgical device. The futility of performing vagotomy for ulcerative colitis has been established since then.

The colon is a useless appendage. It can be excised without being missed. As one of the discussers said, only 350 to 500 c.c. of fluid a day passes the ileocecal valve. The right half of the colon and the terminal ileum constitute the water wringer of the intestine. Excision of 20 to 30 cm. of ileum together with the right half of the colon is an excellent operation for intractable constipation which I have performed on such an indication twice—and with gratifying results. In April 1942, I did another total colectomy for acute ulcerative colitis. This second patient had a diffuse hemorrhagic ulcerative proctitis as well. But the rectal wall seemed supple and flexible when one applied pressure to it. My proctologic and medical associates opposed my plan of doing a primary ileoproctostomy, saying that "the disease would creep from the rectum into the ileum". What poor prophets we can be when we affect a knowledge to which we only pretend! Ah, I wish you could read the notes on her record written by my proctologic associates! Presently, however, I noted my patient no longer

needed transfusions, and presently too the patient discovered she was better. When two years had elapsed, all proctologic evidence of residual ulcerative colitis had disappeared. I did additional cases and reported them (*Surgery 14*:403-432, 1943) and Toon and I subsequently amplified upon that experience (*Am. J. Surg. 75*:384-404, 1948).

Near or total colectomy is the operation which I prefer for cancer of polyps of the colon, anastomosing either the terminal ileum or the cecum to the rectum. It is an operation which can be done with the same risk as segmental colic resection—less than 5 per cent.

We do see transient diarrhea following near or total colectomy, but upon restriction of water intake, the diarrhea usually comes readily under control. Seventy per cent of dry food eaten is available as water, and if a patient drinks no other fluid than milk and takes a low residue diet, it is astounding how quickly the diarrhea usually subsides.

I was fascinated with what Dr. Fox said about the potassium loss factor in the genesis of diarrhea. Our knowledge concerning its use in the management of diarrhea is of recent origin. In the 1942 edition of Gamble's syllabus—and I suppose Gamble in 1942 was the foremost of students of clinical aspects of the electrolyte problem in our country—yet, his monograph contained no information on potassium. In 1928, Hartman of St. Louis proposed a replacement fluid for infants which contained potassium. Yet, it was not widely used. About the time of the Civil War, in our country, a German by the name of Schmidt wrote a monograph concerning the use of potassium in the control of the diarrhea of infants. It was probably knowledge of the role of potassium in provoking cardiac standstill that led to discontinuance of the administration of potassium to infants in the control of diarrhea. It remained for Dr. Darrow, then of Yale now of the University of Kansas, to resurrect the use of potassium in the control of infantile diarrhea, an agency which Darrow first employed in an epidemic of infantile darrhea in Galveston in 1943.

Ulcerative colitis is a disease in which surgeons should take a more active hand in management. In earlier years, I stood by and watched a colleague's son die under conservative medical management and performed an emergency colostomy for distention, only when it became apparent that peritonitis was present. At autopsy a local perforation was found. It is obvious now with many years of backward vision to guide us, that this patient should have had a primary colectomy. If that had been done then (1937) that boy probably would have been alive today. From a long and large experience all of us learn painful lessons, but the purpose of exchanges like this is to teach us to learn from one another's experience.

It is a tragic thing for a young man to be asked to accept a complete colectomy and proctectomy for ulcerative colitis. We need to probe methods by

which it would be possible to save the rectal sphincters or find some substitute better than an ileostomy. When proctectomy is done, in excising the rectum, the surgeon should hug the bowel wall very closely in order to avoid making a young man sexually impotent. In the female this precaution is not necessary.

I find that young, marriageable women with ulcerative colitis are very anxious to save the rectum, and put up with an anastomosis, even though such a procedure might entail five or six stools a day for a short or even a long period of time. Young men on the contrary are much more likely to ask for an ileostomy and a bag which can be emptied once or twice a day. Ulcerative colitis is a complicated problem involving psychosomatic and psychologic factors and aberrations. The role of the surgeon in the treatment of ulcerative colitis is, I think, an important one. As years go by, I believe that patients, general practitioners and internists will find that early surgery can save lives as well as unnecessary suffering from this ailment.

Recently, I operated upon a woman who had undergone a number of operations for repair of a rectovaginal fistula, which had been present for 14 years and which had followed irradiation and hysterectomy for cancer of the uterus. In my own first attempt I employed the Maunsell-Weir maneuver which Orvar Swenson has adapted to the surgical management of megacolon. I too had used this maneuver successfully in two early efforts with cancer of the rectum in the abdominoanal pull-through method (*Surgery 14*:403-432, 1943). In this patient, however, with great induration of all the pelvic tissues, healing and apposition failed, the bowel retracted and the result was not satisfactory. In thinking this over, in a subsequent attempt I decided to pull the entire remaining colon through the anal orifice after excising the mucosa in the short, remaining rectal segment. With division of the mid-colic artery at its site of origin, it was easy to bring the colon out. It hung almost to the patient's knees. The portion which obviously was not viable, I excised. My thought was that if the bowel could heal in solidly with the sphincters still intact, that continence should be good. Three weeks later, I dismissed the patient after cutting away all but about 20 cm., which still hung out of the anal orifice. Three weeks later, I readmitted the patient for a day and cut off the excess just beyond the anal skin. It withdrew just within the anal canal. It was then found that the patient (who was very cooperative and most anxious to get away from the colostomy which had been present all these years), could hold water enemas very well when injected into the rectum. The colostomy was closed a few weeks later and the patient describes her continence now as being "99 per cent perfect". This was a very happy ending for what had been a very trying illness for this patient. She was still in her mid-forties and the restoration of full rectal continence with omission of the colostomy meant a new life for the patient and her husband.

In the paper of 1943, (*Surgery 14*:403-432, 1943), I reported having done such an operation upon a young boy with ulcerative colitis. I did not, however,

bring out a long segment of the colon leaving it *in situ* until the healing was complete, as was done in the instance of the patient with the rectovaginal fistula reported herein. That experience suggests very definitely that, it might be worthwhile doing the operation in the same manner as was done in the patient with the rectovaginal fistula. Failure can be discouraging, but it should also provoke us to seek methods to find our way around it.

Dr. Barowsky:—I should like to ask you two questions. 1. How early would you do a total colectomy? 2. Do you prefer anastomosis of the ileum to the rectum, and what has been your experience with these ileostomies, permanent ileostomies?

Dr. Wangensteen:—It is difficult to answer Dr. Barowsky's questions directly. How early should colectomy be done? Well, if the patient comes in with fulminant ulcerative colitis with picket-fence fever, that is the time to take the colon out. And if the rectum is uninvolved, the procedure of election would be to anastomose either the ascending colon (a few cm. beyond the ileocecal valve) or the ileum to the rectum or to the iliac colon, a few cm. distal to the sacral promontory. One would not choose an ileostomy life—moreover, an ileostomy needs care. With a Perry-type of disposal bag, however, patients having an ileostomy can carry on a fairly normal existence. I have begun to reexamine the possibility of making a continent anal ileostomy along the lines that I described several years ago (*Surgery*, **14**:403-412, 1943), with the added precaution of making studied efforts to provide firm healing between the extruded ileocolic segment and the rectal wall. I have the feeling that this method deserves a retrial.

Concerning the second case, do we have evidence beyond testimony that this patient did have ulcerative colitis? Is there a film of the colon, which we could see? What of the proctoscopic findings? The patient has achlorhydria. Is it possible that the second patient had a colectomy for some other diarrheal disease? As a clinician I am a doubting Thomas until I have seen the evidence. I would like to "stick my finger in the wound" here.

Dr. Barowsky:—We have a report from the other hospital that this was ulcerative colitis, and they did a rather rapid excision of the colon after just a few months' diarrhea.

Dr. Wangensteen:—Is the lady here? I would like to see her. I would like to inspect the ileostomy.

Dr. Barowsky:—If you look at the history, you find that the disturbances in nutrition and electrolytic balance are much more marked than in the previous case.

(Examination of patient.)

Dr. Barowsky:—Now that you have examined the patient, Dr. Wangensteen, have you additional comments to make?

Dr. Wangensteen:—It looks like a very good ileostomy and the mucosal orifice is good. There is no stricture. Stricture of an ileostomy is a frequent cause of diarrhea, as is a strictured anastomosis. Following near or total colectomy, a patient with a patulous anastomosis, rarely, if ever, has diarrhea, unless ileum was sacrificed in the operation. If there is a stricture, diarrhea is very common. That is not the cause here. The patient obviously has a hypermotile bowel, for some reason or other. Possibly the capacity of the ileum to absorb water is impaired—at least for the present.

This sort of occurrence, as it is outlined here, occurring during early convalescence, is not extraordinary. I have seen it on many occasions, but for it to recur as here a year after operation, in my experience is unusual. Perhaps there has been some other contributory circumstance that has brought this complication about; or, perhaps she has become the victim of a vicious circle, with loss of potassium, sodium, and calcium, with continuance of the diarrhea. At the moment, as far as I can see, she has gotten back on her feet again.

It would look as though little defections, here and there, have worked in a symbiotic fashion to bring her close to death. And you have revived her with replacement therapy. The important thing now is to try to keep her on an even keel. Whoever is responsible for her care will have to see her about once a week, at least, until she can go on her own.

Dr. Barowsky:—Dr. Fox, will you make some comments?

Dr. Fox:—Some of the comments which one might make are in this abstract which I have had mimeographed for you, on Potassium Metabolism in Gastroenteritis*, and contains some material from the *Nutrition Reviews* for this month.

The lantern slides and much of the discussion are taken from the following references:

Gamble, James L.: Lane Medical Lectures: Companionship of Water and Electrolytes in the Organization of Body Fluids. Stanford University Publications; Medical Sciences, **5**: No. 1. 1951 (See especially parts II and III).

Darrow, D. C.: Therapeutic Measures Promoting Recovery from the Physiological Disturbances of Infantile Diarrhea. Pediatrics, **9**:519, 1952.

Fox, Charles L. Jr. and Lasker, Sigmund E.: Fluid Therapy in Surgical Emergencies including Hemorrhage, Loss of Gastrointestinal Fluids, and Thermal Burns. S. Clin. North America, **35**:335 (April), 1955.

*Potassium Metabolism in Gastroenteritis: Nutrition Rev. (Oct.), 1956.

Dr. Barowsky:—We will now discuss some of the therapeutic measures we employed to delay gastrointestinal motility and to compensate for some of the water and electrolyte losses. Dr. Fox, will you please say a few words about the correction of water and electrolyte disturbances in this patient?

Dr. Fox:—With the loss of fluid, electrolyte replacement was a big job. I think the composition of the stool gives you a clue as to what is needed. The sodium in the stool is even higher than that in the plasma. They usually are similar to one another, so the water administered by way of replacement needs to contain the same level of sodium. The chloride is also considerable, so the replacement should contain both sodium and chloride in plasma-like concentration. Extra potassium would be essential.

I think the volume needed would be very difficult to estimate, and here the urine chemistry is of some help. There is no sodium detectable, you notice, in the urine. I think it is necessary to administer sufficient balanced electrolyte solution, (which is a plasma-like solution in terms of its inorganic salt and water composition) until one begins to see some sodium appearing in the urine. I would doubt that one could achieve normal electrolyte compensation of the body fluids until there was some sodium in the urine. Ordinarily when there is a reduction in the sodium levels in the body fluids, sodium is one of the first values to drop to practically nil, which you see here.

Potassium continues to remain high in the urine. Because of the difficulty of administering high levels of potassium intravenously, it is probably essential to give additional potassium by mouth. I think it would be difficult to replace all the potassium needed intravenously, because of the danger of hyperkalemia, which could be fatal. Administration of calcium (as calcium lactate) by mouth would help correct the calcium deficit. It is interesting here to see that the level is 6 mg. per cent, which is extremely low. There is often considerable loss of calcium through the stool, which would bring the level to that low figure.

I don't know whether you found rarefaction of the bone on bone x-ray.

Dr. Barowsky:—We did. That is why I wanted to demonstrate it roentgenographically.

Dr. Craig will now show the change in motility by comparing the gastrointestinal x-ray series before and during therapy.

Dr. Craig:—(Films) The top center x-ray is the gastrointestinal film taken in September 1956. The barium shows nothing abnormal in the stomach, and I wouldn't call the small intestine abnormal except for the terminal ileum. It is somewhat dilated here. Here is the ileostomy opening, and you notice barium flowing out of the opening.

Dr. Barowsky:—What was the time element?

Dr. Craig:—Five hours. There is still an amount of barium remaining in the stomach, but for that small amount of barium I wouldn't call it terribly abnormal.

Dr. Barowsky:—At first Demerol 100 mg. t.i.d. was used to control the diarrhea, but this was not too effective. I know from my own experience and the work of others, that very marked delay in transit both through the stomach and small intestine can be attained if you employ relatively large doses of anticholinergic drugs. We gave this patient twice the standard dose of Pro-Banthine. Dr. Craig, will you show us what happened to this patient?

Dr. Craig:—(Film) Following the ingestion of barium there is some gastric retention of one, two, three, four, five, six, and seven hours.

Dr. Barowsky:—As much as seven hours.

Dr. Craig:—After seven hours you should expect a greater flow of barium in the small intestine than you see in this case. There certainly has been a marked delay in gastric and small intestinal motility.

Dr. Barowsky:—This patient also had a gastrocolic reflex mechanism. Immediately after ingestion of food, she would have diarrhea. Administration of Pro-Banthine arrested this mechanism. She is relatively comfortable now, her peristomal inflammatory reaction is subsiding.

Question:—Can you give us the dose of Pro-Banthine used?

Dr. Barowsky:—The Pro-Banthine dose was 30 mg. orally, one hour before meals and before retiring.

Dr. Snapper:—In general too large quantities of fluid are given intravenously. This is clearly demonstrated at the autopsy table where many patients prove to have edema of the brain, edema of the lungs, and left heart failure. If one checks the chart of such patients, it always transpires that such patients have received many liters of fluid parenterally. Except for rare cases—especially of diabetic coma—not more than 3,000 c.c. of fluid should be given by vein in the course of 24 hours.

Dr. Barowsky:—Dr. Glass will now demonstrate any disturbances in absorption which may exist in this patient by doing a cobalt-tagged B_{12} test.

Dr. Glass:—As you probably know, the absorption in various parts of the gut is different, and various elements are absorbed at different rates in various parts of the intestine. Vitamin B_{12} is absorbed in the duodenum, jejunum, and possibly also ileum, dextrose is absorbed in the first half of the jejunum, and fats are absorbed in the lower three-quarters of the ileum; depending on whichever part is resected the absorption will be accordingly impaired. If we resect the upper part of the small intestine, we will have a defect in absorption

of iron, and Vitamin B_{12}. If we resect the lower part alone, we will have a defect in absorption of fats and Vitamin B_{12}. If we resect the right colon–defective absorption of water and sodium will result.

If you take two different types of patients: on one side, one with resected small intestine–we had such a case, which I have on the slide, and one with resected colon–like the one we have here–and you give them radioactive Vitamin B_{12} by mouth, and follow what happens to the Vitamin B_{12} absorption –you will find two different patterns. If a large part of the small intestine is resected, Vitamin B_{12} will not be absorbed or only in traces. If colon is resected, even totally, B_{12} absorption will proceed normally.

We can detect the absorption of the radioactive B_{12} by the following technic, which we devised: A small tracer dose of $CO^{60}B_{12}$ is given by mouth; 24 hours later castor oil and next day enema are administered, and 48 hours after the administration of the tracer the radioactivity of the liver is measured by external scanning with scintillation counter in a similar way as the radioactivity of the thyroid is measured after the administration of radioactive iodine. If we give radioactive B_{12} to the patient with resected small intestine, Vitamin B_{12} will not be absorbed and you will find no radioactivity over the liver. If you give it, however to the patient with resected colon, he will absorb B_{12} very well, which will show as a positive hepatic uptake of radioactivity.

This slide shows data on hepatic uptake of radioactive $CO^{60}B_{12}$ in three groups of cases, after the oral administration of a tracer dose of one-half of microgram of B_{12} containing one-half of a microcurie of $Cobalt^{60}$. In colitis and irritable colon the hepatic uptake of $CO^{60}B_{12}$ is at a normal rate. If, however, one gives $CO^{60}B_{12}$ orally to sprue patients, who cannot absorb Vitamin B_{12} because they have developed a B_{12}-absorption defect in the intestine, they will show no counts over the liver. If you add the intrinstic factor preparation to B_{12}, they will still have no counts over the liver, because the absorption defect in sprue does not depend on the lack of intrinsic factor, as is the case in pernicious anemia. If you add the intrinsic factor to B_{12} and give it to the patients with pernicious anemia, they will behave like normal people, and the B_{12} absorption defect will be corrected.

Here are two cases of regional enteritis which behave similarly to sprue. The second case is the one which I just mentioned: The patient was studied several times, first time–before the operation. Then she was examined after one segment of ileum was anastomosed to another ileal segment, and the ileitis was left *in situ*. Finally, she was studied for the third time, after almost the entire small intestine, with the exception of the first three and a half feet, was taken out. At that time therefore, this patient had only three and a half feet of the jejunum left. B_{12} absorption was in traces but certainly better than when the patient was in the acute stage of the disease, with entire length of small in-

testine preserved. This means that those three feet of small intestine could still absorb some amount of Vitamin B_{12}, which it could not do before, during the acute stage of disease. Anyway, B_{12} absorption in patients with regional enteritis is severely impaired, like in sprue. The patients may, therefore, easily develop macrocytic anemia.

We studied by the same technic this patient with totally resected colon, and found that she had a very high hepatic uptake of radioactive B_{12}, somewhere in the range of the maximum values. This means that without the colon the patient absorbs Vitamin B_{12} in a normal way. Therefore, we don't have to expect any macrocytic anemia in cases of resected colon, which is in contrast to patients with resected small intestine.

If you want to see the technic, we have the set-up in the other room and we shall be glad to show it to you.

(The patient was removed to another room for the demonstration.)

CLINICAL ASPECTS OF PARASITIC INFECTIONS OF THE GASTROINTESTINAL TRACT*

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This lecture will concern itself with three topics in the field of parasitology of current, practical interest to the clinician. They are—the place of quinacrine in the treatment of tapeworm infection, the comparative value of various specifics used in amebiasis, and the diagnosis and treatment of *Schistosoma mansoni* infection.

Treatment of Tapeworm Infections

The use of quinacrine (Atabrine) for the treatment of tapeworm infections was introduced by Neghme and Faiguenbaum[1] during the second World War, because of the shortage of male fern preparations. Their trial of the drug in *Taenia saginata* infections was based upon experience reported by Culbertson[2] with a tapeworm infection of mice. Several enthusiastic reports appeared subsequently in Spanish language medical journals. Among them was that of Hernandez Morales[3] from Puerto Rico. He obtained cure in 23 of 24 patients infected with *Taenia saginata*. There was one serious untoward result, an acute psychosis.

While the publication of Hernandez Morales was also available in English, few physicians in the continental United States were aware of the method until Sodeman and Jung[4] published a report of success in all of 11 patients with beef tapeworm infection. One patient had to be treated twice. On the basis of this small series, they concluded that quinacrine was superior to oleoresin of aspidium.

Early experience of the author was briefly cited by Brown[5]. There was complete success in the first 8 cases. Among 34 patients with *Taenia saginata* infection treated with quinacrine between 1947 and 1954, however, the scolex was obtained in only 21 with the first treatment. In the remaining 13 patients, follow-up showed that 6 were no longer passing segments in the stools after a minimum period of 6 months. It is known that, if treatment has been unsuccessful, segments will again be passed within 4 months. Thus, a total of 27 patients, or 79 per cent were cured with one treatment. Of the 7 patients in whom the first treatment failed, 4 were given a second treatment and 3 were cured.

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In 1950 Faiguenbaum and Donckaster[6] reported success in 77 per cent of 56 patients with one quinacrine treatment. Since oleoresin of aspidium results in cure in about 75 per cent of cases, the conclusion that quinacrine is superior appears unwarranted. Rather, it should be stated that the two drugs are about equal in effectiveness.

Quinacrine has two advantages: 1. It does not have to be fresh to be effective. 2. It frequently results in the delivery of a complete worm with the scolex firmly attached. Thus it is especially useful when a whole specimen is desired for teaching or special investigation.

Quinacrine has two disadvantages: 1. There is an attack of nausea and vomiting 4 to 5 hours after therapy in 40 per cent of patients. 2. It may cause an acute psychosis. This has been reported once in the literature[3], and there is at least one unpublished case in a series of 25 patients treated in Canada.

In using quinacrine in the therapy of tapeworm infection one must appreciate its limitations, and above all, realize that it will not always cure the patient.

For adults, the method of treatment is as follows:

1. Nothing but water is ingested after lunch of the day preceding treatment.

2. On the evening of the same day, a cleansing enema is given.

3. Early the next morning, the patient takes 0.8 gm. of quinacrine hydrochloride in 4 doses of two tablets each over the period of a half hour.

4. One hour after the last two tablets, a saline purge is given. The patient is kept at rest except for bathroom privileges for the entire day, and no food is allowed until the purge has taken effect.

5. Only uncoated tablets of quinacrine are used.

Neither quinacrine nor oleoresin of aspidium is usually successful in children, because the dose must be reduced in proportion to body weight for fear of toxic effects. Children usually vomit even when the dose of quinacrine is so reduced.

Quinacrine is equally effective in *Diphyllobothrium latum* infections. Cure has been obtained in 13 of 16 patients with one treatment, and in 2 more with a second. On the other hand, it proved ineffective in 3 cases of *Hymenolepis nana* infection.

Quinacrine therapy is usually contraindicated in patients with heart disease, severe debility, or marked neurotic tendencies.

Treatment of Amebiasis

During the last ten years, practitioners of medicine have been presented with a bewildering array of new antiamebic drugs. Many of the data published in support of their effectiveness are unsatisfactory. Often the report starts with the assumption that there is no satisfactory amebacide. Or, worse, the author selects from the extensive literature a few pessimistic reports and ignores other more optimistic and still reliable reports. In addition, it is usual to have reports on new amebacides published without any comparison of the results with those obtained with more standard drugs in similar patients.

Some perspective on the effectiveness of the newer drugs is provided by a review of the author's experience between 1944 and 1950 with a group of older standard intestinal amebacides. The results obtained in patients 15 years of age or older, with mild amebiasis, were as follows:

TABLE I

Drug	Patients Treated	Failures	Failure Rate
Carbarsone	279	16	6%
Diodoquin	214	15	7%
Chiniofon	84	14	17%
Vioform	83	11	13%

There is no significant difference between the results obtained with carbarsone and Diodoquin. Since the incidence of adverse effects with carbarsone is distinctly higher, Diodoquin is the preferred drug.

Vioform and Chiniofon are definitely less satisfactory. In the case of Chiniofon, the fact that adequate doses (0.75 to 1.0 gm. three times a day) often produce diarrhea makes it necessary frequently to reduce the dose below the effective level. The failure rate with Vioform is the same with twice the recommended dose (0.5 gm. three times daily for 10 days) as with the standard dose (0.25 gm. three times a day for 10 days). Vioform is being widely advertised to travelers for use in diarrhea, including that due to amebiasis. Actually, if any drug of the iodine-quinoline group is to be recommended for self-medication, it should be Diodoquin. The writer believes, however, that the whole concept of suppressive medication for amebiasis is open to question.

The arsenical group of amebacidal drugs now includes Milibis (Bismuth glyconylarsanilate) and Balarsen (Arsthinol) in addition to carbarsone. To assess the value of the newer drugs it seems logical to compare them with carbarsone. Of 36 individuals who received the dose of 0.5 gm. of Milibis three times a day for 8 days, 32 were apparently cured. This means a failure rate of 11

per cent, which is certainly no better than the 6 per cent obtained with carbarsone. Side-effects are as frequent with Milibis as with carbarsone, so it appears to offer no advantage. One case of jaundice was seen among 79 patients treated with Milibis and only two among 458 treated with carbarsone.

Most and his associates[7] report 12 per cent failures in a series of 167 patients treated with Balarsen. Disturbing side-effects occurred in 12 per cent of this series, so that Balarsen appears to be no more satisfactory than carbarsone.

Most of the orally administered antimicrobial substances of the so-called antibiotic group have been tried in amebiasis. It is probable that these substances act indirectly by depressing the intestinal bacteria upon which *Endameba histolytica* depends for its persistence and progress in the colon. Chloramphenicol and neomycin have little value. Chlortetracycline and oxytetracycline are among the most effective of this group. Work done in Korea suggests that oxytetracycline is superior, but reports from South Africa and personal experience indicate no difference if comparable doses are used.

Many individuals, however, will not tolerate 2 gm. daily of chlortetracycline. In fact, both chlortetracycline and oxytetracycline have the distinct disadvantage in mild amebiasis of sometimes producing more gastrointestinal complaints than they allay. Tetracycline itself appears less effective than its derivatives.

Bacitracin treatment of amebiasis has resulted in failure rates between 20 and 30 per cent in mild amebiasis. There is, at present, no preparation on the market suitable for oral administration in amebiasis. No evaluation of erythromycin and carbomycin is offered because the writer has no personal experience with them.

Empirical use of small doses of orally administered antibacterial substances for diarrhea is to be decried, since it often results in suppressing amebic infections to the point where laboratory diagnosis is difficult or impossible, without curing them.

Fumagillin, marketed under the trade name of Fumidil, is an antibiotic which has a direct amebacidal action and no important antibacterial action. The experience of the writer to date indicates a failure rate of about 10 per cent in mild amebiasis. It has two disadvantages as a primary treatment for amebiasis. First, in some patients it causes abdominal burning, abdominal pain, and/or diarrhea, and these symptoms may be sometimes severe enough to require discontinuance of the drug, and, second, it does not provide prompt symptomatic relief where colitis is moderately severe, probably due to its lack of antibacterial action. It has, however, proven successful in cases in which *E. histolytica* persists after symptoms have been partially or completely relieved by other therapy. It is probable that it will prove a useful addition to the antiamebic drugs.

Recent reports on Glaucarubin[8] extracted from a Mexican plant, indicate a failure rate sufficiently high to suggest that it will not replace those drugs already discussed.

Considering both effectiveness and freedom from untoward effects, Diodoquin appears to be the best single drug for amebiasis as seen in this part of the world. In all but the mildest cases, however, it is probably wise to give more than one drug, since there is no perfect amebacide. It is important to bear in mind that, in any individual case, a statistically less effective drug may nevertheless be the successful one.

In the treatment of hepatic amebiasis, Chloroquine (Aralen) has largely, but not completely, supplanted the more toxic emetine.

Schistosomiasis

In this day of interest in the problems of chronic disease, it is strange to report that scores of United States citizens are dying each year of a chronic infection of which the causative agent is known and readily identified, and for which a cure is available. The disease is schistosomiasis, due to *Schistosoma mansoni*.

Schistosoma mansoni is a blood fluke infection acquired from contact with fresh water containing infected snails. There are many endemic foci in the Commonwealth of Puerto Rico. In some the prevalence reaches 40 per cent. Surveys conducted in two New York City hospitals in 1955 and 1956 suggest that the prevalence of the infection among Puerto Ricans exceeds 10 per cent. This agrees with the findings reported from Puerto Rico itself[9]. In other words, there are probably more than 50,000 infected individuals in this city alone.

The adult worms live for the most part in the tributaries of the portal vein. Eggs are deposited in small venules. Some enter the tissues of the colon; others reach the liver and settle in the periportal spaces. In both places they give rise to a granulomatous inflammation which results in fibrosis. In the liver, the periportal fibrosis leads to splenomegaly and other manifestations of portal hypertension. The most frequent cause of death in this disease is hemorrhage from varices in the esophagus or stomach. This late phase of the disease usually takes 10 to 20 years to appear. The parasites may live as long as 35 years, so that the disease progresses even though the patient leaves the endemic area. Routine examination of all exposed individuals and treatment of those found infected will prevent the late fatal complications. In addition, it will often improve the general health of the individual.

Diagnosis of the infection can be made by examination of either the stool or a piece of tissue from the rectal mucosa for the presence of the typical lateral-spined eggs. A simple direct examination of a smear obtained from the feces will detect only about 10 per cent of cases. It is necessary to concentrate

the stools by one of several methods. Obviously, it is also important for the technician to have necessary training in parasitology. More than one specimen of feces should be examined if the first is negative. Approximately 15 per cent of the cases which can be diagnosed if three specimens are examined will be missed if only one specimen is tested. The use of the rectal biopsy for the diagnosis is often misunderstood. If the tissue removed is sent for routine histological examination, the results will be less satisfactory than those of a careful stool examination. The tissue removed should be teased out in tap water and examined whole under the low power of the microscope. Some workers feel that this method is to be preferred to stool examination. Recent work by Spingarn and co-workers[10], indicates that its efficacy may be overrated, since they found only a slightly higher yield with this method as compared with stool examination. More important, they report that in 7 of 100 cases, diagnosis was made by stool examination but not by rectal snip.

Which patients should be examined for schistosomiasis? Ideally, tests should be carried out on all individuals who have lived in Puerto Rico, or other known endemic areas. But it is of some interest to the clinician to know what symptoms may occur in schistosomiasis before the late state of portal hypertension. There may, of course, be no distinct symptoms. Abdominal pain, diarrhea, and blood in the stools, and weakness and tiredness, however, are features frequently found in the earlier periods. Heavy infections may produce a profound febrile illness in the weeks immediately following their acquisition. Neurological and cardiopulmonary manifestations may occur exceptionally.

Any Puerto Rican patient sick enough to be admitted to a hospital should be studied for schistosomiasis, whatever his symptoms, but most especially if he has any gastrointestinal symptoms, eosinophilia, or enlargement of the liver or spleen, or chemical evidence of liver dysfunction.

Schistosoma mansoni infections are treated with intramuscular injections of stibophen (Fuadin), a trivalent antimony compound. After test doses of 1.5 ml. and 3.5 ml. on successive days, a person who weighs over 100 pounds should receive 5 ml. every other day until a total of 70 to 100 ml. is reached. Patients under 100 pounds should receive a total of 1 ml. per pound, divided into 20 doses and preceded by small test doses. The patient must be watched carefully for important toxic effects. These occur in the skin, kidneys, gastrointestinal tract, joints, and rarely the heart. Recurrent vomiting, progressive albuminuria, and symmetrical skin eruption require modification or interruption of therapy. Minor changes in the electrocardiogram are frequent and can be ignored unless there are clinical manifestations such as precordial pain or arrhythmia. The presence of heart disease is a contraindication to therapy.

Stools should be re-checked periodically for one year after treatment to determine whether the patient has been cured.

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Discussion

Dr. I. Snapper:—Everybody will have enjoyed the excellent presentation of Dr. Shookhoff. Personally I am not in favor of using an arsenical compound for the treatment of amebiasis as long as other less dangerous drugs are available. Many arsenicals used for amebiasis occasionally give rise to a transverse myelitis. Although this complication fortunately occurs only very rarely, I still do not feel justified in treating a relatively innocent disease with a drug which may give rise to such a dangerous side action.

I have used Diodoquin with excellent results for the treatment of amebiasis in this part of the world. Unfortunately it is expensive and can therefore not be used in the Orient. In addition, Diodoquin which is hardly absorbed from the intestine, has no influence upon hepatitis. Emetin injections, which are not expensive, are still the favorite therapy for amebiasis in the Orient. Ten or fifteen subcutaneous injections of one grain of emetin have, in my experience, never given rise to any complication as far as myocardial damage is concerned. Emetin does not only work upon the intestinal form of amebiasis but also in amebic hepatitis. Anybody who is—unjustifiably so—afraid of emetin can of course use Chloraquin for the treatment of the liver complications of amebiasis.

Whether the antimony treatment of liver cirrhosis due to schistosomiasis is very effective, remains to be seen. It is always remarkable how few worms and eggs are found at the autopsy of patients with liver cirrhosis due to schistosomiasis. It seems that the liver degeneration which develops under influence

of schistosomiasis, is a self-perpetuating process. Once the disease has started it follows a fixed course and it seems improbable that the killing of a few schistosomas will save the liver parenchyma. In addition, it cannot be denied that after the treatment with doses of Fuadin, which nowadays is popular, occasionally an antimony death occurs. This is usually the case in young Puerto Ricans with schistosomiasis who have been anemic for a long time and must have developed a fatty degeneration of the heart muscle. If such a young and skinny individual receives the same doses of Fuadin as are customarily administered to husky young Americans, then myocardial degeneration may well result.

THE POSTBULBAR DUODENAL ULCER*

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and

HARRY J. KANIN, M.D.‡

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Introduction

The diagnosis of gastric and duodenal ulcer has attained a high degree of accuracy. A peptic ulcer occurring elsewhere in the digestive tract is not diagnosed as readily. In a comparison of autopsy statistics and clinical studies it becomes apparent that postbulbar duodenal ulcer is not diagnosed often enough.

In 1947 Alvarez and Farinas[1] noted that the postbulbar duodenal ulcer received scant attention in medical literature and it was generally looked upon as an unusual finding. They also observed that this lesion was frequently overlooked because of difficulty in examining the postbulbar region in the ordinary radiographic examination and failure to keep the possibility of this lesion in mind.

The situation has not changed and we believe the same observations can be made today.

Incidence and Historical Aspects

Alvarez and Farinas[1] made a careful summary of the historical background and the development of interest in the postbulbar duodenal ulcer. The reader is referred to their very fine discussion of the subject.

Symptoms

The symptoms of postbulbar duodenal ulcer are in no way characteristic and a clinical diagnosis is not possible.

Lonergan and Kahn[3] have found that pain was the most frequent complaint and bleeding second in frequency.

The pain differs very little from that encountered in bulbar ulcers. The pain may be associated with fullness or bloatedness. Samuel[5] has noted that the pain tends to radiate to the back and to the right scapular region and that the

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ulcer shows a tendency to penetrate usually into the pancreas. There is a less noticeable food pain relationship. The food does not seem to ease the pain as in the usual bulbar ulcer. Nocturnal pain has been noted in a high percentage of patients. Alkalis have given only transient relief. Obstructive symptoms have occurred but they are not frequent. Robinson[4] noted that the symptomatology varied and was frequently atypical and emphasized gaseous distention, postprandial eructations and nocturnal epigastric pain.

The hemorrhagic tendency was stressed by many observers. Swarts and Rice[7] stated:

"It appears that although postbulbar ulcer is much less frequent than ulcer of the duodenal cap, it is more often serious, in that the tendency to bleed is much greater. We, as well as others, have been impressed by the high incidence of intractability in these cases".

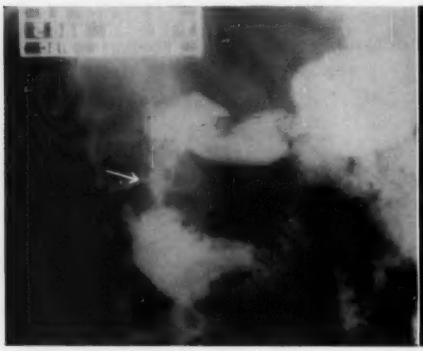

Fig. 1

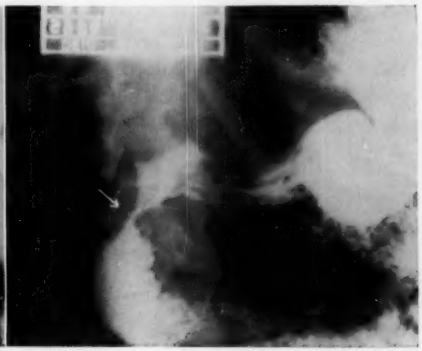

Fig. 2

Fig. 1—Case 1 before treatment.
Fig. 2—Case 1 after treatment.

Some of the postbulbar duodenal ulcers show a tendency to penetrate posteriorly into the pancreas. These posterior wall ulcers with penetration constitute an important part of the group of intractable ulcers.

Shaiken[6] has noted that the postbulbar ulcer must be included in that group of special types of peptic ulcer like the jejunal ulcer which show an almost natural tendency towards intractability.

Diagnosis

The diagnosis is generally made on roentgen study. Occasionally the diagnosis is made at surgery or autopsy.

Ball, Segal and Golden[2] have emphasized that postbulbar ulcers are seen best in an exaggerated oblique view with the patient lying on the right side in

a horizontal position. The best position is determined on fluoroscopy which permits the most satisfactory lengthening-out of the upper duodenum. The Trendelenburg position is sometimes helpful and a pressure cone may be used to uncover a segment. The most significant finding is the demonstration of a crater. The crater may be found on either border or the anterior or posterior wall of that portion of the duodenum extending from the distal end of the duodenal bulb to the ampulla. Most frequently the crater is found on the medial border. The crater must be present constantly to be significant.

Differential Diagnosis

The clinical differentiation of postbulbar and bulbar duodenal ulcer based on symptomatology is not possible.

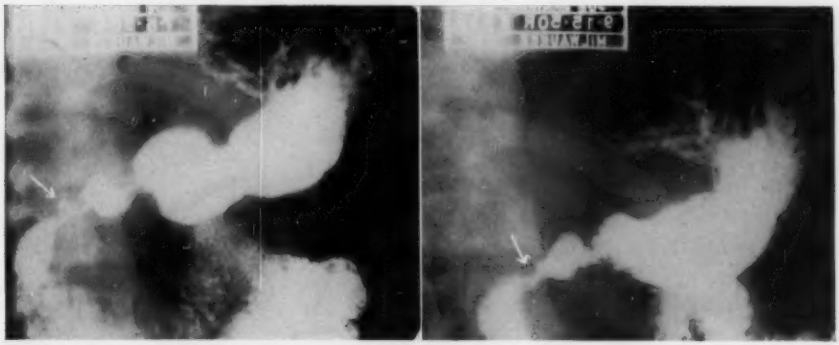

Fig. 3 Fig. 4

Fig. 3—Case 5 before treatment.
Fig. 4—Case 5 after treatment.

The following lesions must be considered in differential diagnosis:

1. Duodenal diverticuli,
2. Duodenal neoplasms,
3. Duodenitis,
4. Pancreatic lesions,
5. Parasitic infestations,
6. Hypertrophy of Brunner's glands.

1. The typical duodenal diverticulum with its well-defined rounded borders and narrow neck will usually be easily recognized. Longitudinal folds found in

the neck of the sac will help in diagnosis. At fluoroscopy the diverticulum may be seen to fill and empty and it may change in size while under observation. There is usually no associated duodenal irritability. A medical trial of ulcer treatment with subsequent examination to note a reduction in size or disappearance of the lesion may be necessary in some patients to differentiate between an ulcer and a diverticulum.

2. A filling defect with irregular margins and infiltration of surrounding structures suggests a neoplasm. The differential diagnosis may have to be established at surgery. Duodenal tumors are very rare.

3. In duodenitis the duodenum may show marked irritability. The lumen may be narrowed and the borders show multiple projections or superficial mucosal ulcerations, presenting a serrated appearance. The mucosa may show hypertrophic changes.

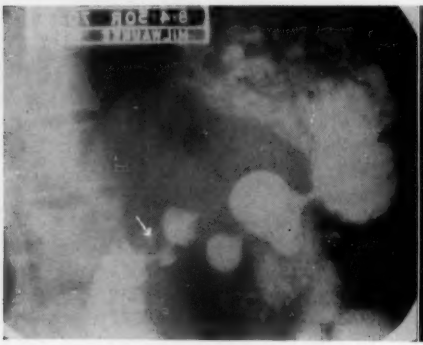

Fig. 5

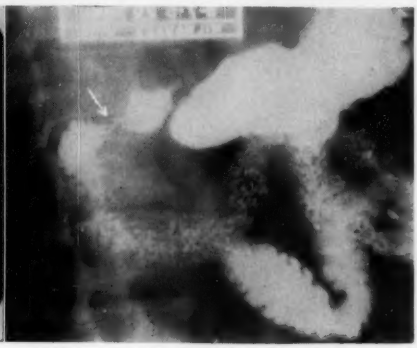

Fig. 6

Fig. 5—Case 6 before treatment.
Fig. 6—Case 6 after treatment.

4. Lesions of the pancreas may offer difficulty in differential diagnosis. The postbulbar duodenum which has undergone stenosis following the healing of an ulcer may simulate the roentgenographic appearance of an annular pancreas or a pancreatic neoplasm. Surgery will have to be considered in these patients. Good clinical progress may aid in deciding whether or not surgery should be done.

5. Hookworm and giardia infestation sometimes produce changes in the duodenum which are confusing. Severe anemia with eosinophilia, and biliary drainage, may aid the differential diagnosis.

6. Hypertrophied Brunner's glands usually produce changes more suggestive of infiltration or hypertrophy than of ulceration.

Review of Patients

Twenty-one patients with postbulbar duodenal ulcer were seen in a period of twenty years and approximately 10,000 consecutive patients. The case histories of seven of these patients is presented as follows.

Case 1:—H. L., a white male, age 53, was seen January 1955. He complained of upper abdominal distress with gas and bloating since November 1954. Night pain was present. Baking soda relieved his distress. An x-ray examination of his digestive tract revealed a large postbulbar duodenal ulcer (Fig. 1).

The patient was placed on an ulcer diet and medications. His response to treatment was good. In March 1955 a repeat study of the upper digestive tract revealed healing of the ulcer crater with a narrowing of the involved portion (Fig. 2). The possibility of further stenosis and obstruction suggested itself but no gastric retention was demonstrated. Surgery was strongly recommended. The patient refused to consider surgical treatment because he felt good.

Case 2:—F. K., a white male, age 35, was first seen in 1946. The patient stated that since 1937 he had had epigastric burning, relieved by food, occurring in the spring and fall of each year. He had gross gastrointestinal hemorrhages in 1939, 1941, 1943, 1945 and 1946. Each bleeding episode was preceded by a recurrence of upper abdominal distress. A diagnosis of postbulbar duodenal ulcer was made and surgery advised. The patient decided that he would defer the surgery but he would follow a strict medical regime. He remained well for five years. In 1951 he had another severe recurrence with a massive hemorrhage. A surgeon was called in consultation. The patient stopped bleeding and again surgery was deferred. About one year later there was another recurrence of ulcer activity and a massive hemorrhage. Multiple transfusions failed to control the bleeding or improve the patient's condition. The patient expired on the operating room table. A bleeding postbulbar duodenal ulcer was demonstrated at surgery.

Case 3:—J. R., a 64-year old white male was seen in April 1950. His main complaint was severe pain which occurred several times each day. He had distress for three years but more severe in the last few months. The x-ray studies revealed a postbulbar duodenal ulcer. An ulcer diet and antacid medications gave very little relief. Codeine failed to control the distress. Surgery was recommended but refused. The patient continued to have severe pain. He finally consented to have surgical treatment. A subtotal gastrectomy was done. The ulcer was found in the second portion of the duodenum penetrating the pancreatic wall. The ulcer was not removed.

Case 4:—A white male, age 43, was seen for the first time in August 1951 with a gastrointestinal hemorrhage. The response to several transfusions of whole blood and a medical ulcer regime was prompt. A gastrointestinal study revealed a postbulbar duodenal ulcer. In August 1952 and in November 1952

the patient had recurrent gastrointestinal hemorrhages. X-ray studies again revealed the postbulbar duodenal ulcer. Surgery was recommended but the patient refused. In November 1953 the patient had another episode of bleeding. Surgery again was refused.

Case 5:—A white, 35-year old male, was seen in July 1950. He had a history of four gastrointestinal hemorrhages between 1948 and 1950. X-ray studies of the digestive tract revealed a postbulbar duodenal ulcer (Fig. 3). A medical regime for ulcer was ordered. In September 1950 reexamination of the digestive tract revealed no evidence of any ulcer (Fig. 4).

In 1952 the patient had another gastrointestinal hemorrhage and x-ray studies revealed again the presence of a postbulbar duodenal ulcer. Surgery was recommended. The patient decided to have surgery done elsewhere.

Case 6:—E. S., a white, 48-year old male, complained of epigastric distress relieved by alkali. The pain particularly was noted during the night. X-ray studies in August 1950 revealed a postbulbar duodenal ulcer (Fig. 5). In October 1950 re-examination revealed complete healing of the ulcer (Fig. 6).

The patient's symptoms recurred in 1952 and the postbulbar duodenal ulcer again was demonstrated on x-ray studies. Surgery was recommended and a subtotal gastrectomy was done.

Case 7:—H. S., a 51-year old patient, was seen by another physician because of shortness of breath. A severe anemia was recognized immediately and the gastrointestinal tract the site of blood loss. The patient was seen in consultation. The hemorrhage was very severe and surgery for a bleeding ulcer was recommended. At surgery the site of bleeding was not found. The patient expired within 24 hours. At autopsy a very small postbulbar duodenal ulcer with an obvious open vessel was demonstrated. The ulcer was just above the ampulla.

Summary

Five patients were diagnosed by x-ray. One diagnosis was established at surgery. In the remaining patient the lesion was missed at surgery and identified at autopsy.

The most striking observation is the tendency toward repeated hemorrhages. Five of these patients had gross bleeding. One patient had nine hemorrhages, another five and a third patient four. The hemorrhages were, as a rule, profuse.

One patient had pain which was intractable to repeated courses of medical treatment. He was operated upon and relieved of symptoms.

Another patient had a good clinical response to medical treatment but developed a marked stenosis following treatment. No gastric retention, however, was noted on roentgen study. Surgery was recommended but refused.

Only one patient responded to a medical regime.

It is well to consider a postbulbar ulcer as an intractable type of ulcer. Surgery should be considered as the treatment of choice in the patient who has bled, who had intractable pain or who shows evidence of obstruction.

Conclusions

The postbulbar duodenal ulcer occurs sufficiently often to warrant serious consideration in differential diagnosis, particularly in patients with repeated gross hemorrhages, intractable pain or obstruction. The lesion is underdiagnosed. It must be looked for to be found.

Hemorrhage is the most frequent and most serious complication. Two of our patients died from exsanguination, one in the operating room and the second after the lesion was missed at surgery and found at autopsy.

Intractable pain is the second most serious complication. These intractable ulcers are usually the result of walled-off perforation.

In our experience medical treatment is usually unsatisfactory.

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Discussion

Dr. I. Snapper:—We must compliment Dr. Shaiken and Dr. Kanin for their excellent demonstration on the postbulbar duodenal ulcer. Although this is a rare disease it is an important one because it certainly will often require surgical treatment.

Hookworm disease may also cause postbulbar duodenal ulcers, but fortunately this disease does not occur often enough in the United States to cause differential diagnostic difficulties.

Dr. O. H. Wangensteen:—I should like to ask Dr. Kanin two questions:

1. How far beyond the pylorus and the pyloric canal did these ulcers occur?

2. What kind of surgery was done?

Dr. Harry J. Kanin (Milwaukee, Wisc.):—The closest we have come to seeing hookworm disease of the duodenum is seeing it mentioned in the literature.

By definition, the postbulbar ulcer is that ulcer which occurs in the area of the duodenum between the distal end of the duodenal bulb and the ampulla. Of course, technically any peptic ulceration occurring beyond the ampulla is a postbulbar ulcer, but for practical purposes most of these ulcers occur in that area.

The surgery that is performed is the subtotal gastrectomy in these cases. In one patient, of course, that was very unsuccessful. The patient continued to bleed from the postbulbar ulcer, and died.

Dr. Wangensteen:—Was it a Billroth II?

Dr. Kanin:—I don't know what particular operation was performed on this patient. I was not associated with Dr. Shaiken at that time. The reason why the ulcer was not resected was simply that it was not thought of as being present in that area. As you probably could very well tell us better than I can, to resect an ulcer in this region is technically a very difficult procedure. The ileum is frequently inflamed and there is a swollen area near the ampulla of Vater and common duct, and frequently you have to content yourself with the subtotal gastrectomy, hoping that the anacidity produced will allow the ulcer to heal.

Dr. Wangensteen:—I should like to make one more comment if I may. I think the radiologists diagnose postbulbar ulcer far more often than it occurs. In doing segmental resection, which is my operation of choice for duodenal ulcer, I regularly perform a Heineke-Mikulicz pylorotomy. I cannot recall having to extend the pylorotomy incision down into the ampullary region to come within range of the ulcer. In fact, most duodenal ulcers lie immediately beyond the pylorus. The suggestion that duodenal ulcers are found in the juxta ampullary region, in my experience, suggests that such roentgen findings may be in part an optical illusion.

It was for technical reasons that I first adopted segmental resection in the surgical management of duodenal ulcer. I did not then know how good an operation it was going to prove to be. When one cuts the anterior duodenal wall longitudinally in a difficult duodenal ulcer, it is easy to close it transversely. If hemorrhage happens to be present, the bleeding vessel is found and stitched. Then one opposes the adjacent mucus surface over the ulcer crater with a few interrupted silk sutures. When the pyloroplasty is completed, a 35-50 per cent excision of the corporic mucosa completes the operation. In fact, when the antrum is left, one can excise safely less fundic mucosa to prevent recurrent ulcer than in the Billroth operation in which the antrum is sacrificed regularly. Segmental resection has had a bad name. It was used by Continental surgeons

50 years ago in the management of gastric ulcer. They failed to understand that transverse division of the stomach vagotomizes the antrum causing gastric retention. I too had to learn this lesson independently in 1949. The addition of a pyloroplasty made segmental resection a first-class operation—one which I invoked for the surgical relief of duodenal ulcer. It is apparently important to denervate the antrum in doing segmental resection—a lesson which my colleagues and I had to learn from experience with tubular resection. Such can be the value of experience with tubular resection. Such can be the value of experience critically examined.

We have discontinued tubular resection in this clinic, because we have seen 2 bona fide recurrences in 200 such operations. We probably will see more, because the first tubular resection was done less than 5 years ago. We have observed no recurrences in segmental resection, and the first such operations were done in this clinic more than 8 years ago.

THE SIGNIFICANCE OF THE GASTRIC SECRETION AFTER PARTIAL GASTRECTOMY AND GASTROENTEROSTOMY*†

With Description of a Method for Determining the Acid Output

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The gastric acidity after partial gastrectomy has been previously investigated by both fractional analysis and quininium exchange resins. Winkelstein's[8] study included a comparison of the gastric acidity in response to gruel with that of gruel and histamine stimulation in patients in whom gastrectomy had been carried out for duodenal and gastric ulceration, and Cornell and Druckerman[15], utilizing gruel, gruel and histamine, and other methods of stimulation, determined the gastric acidity some months or years after gastrectomy in a similar group of patients. Shay[1] stressed the importance of appraising the true gastric acidity after gastrectomy. He measured the acidity in response to the Ewald test meal, electrometrically where no free acid was detectable by Töpfer's reagent in specimens obtained by intermittent aspiration of the gastric contents through a Rehfuss tube, the tip of which was adjusted under radiological control to lie just above the stoma. All these workers[1,8,15], reported a rather high incidence of achlorhydria in patients after gastrectomy. This was probably due, in part at least, to mildness of the secretory stimulus employed and duodenojejunal regurgitation. The unsuitability of the tubeless method for determining gastric acidity in the stomach remnant of patients after partial gastrectomy has been demonstrated by Shay, Ostrove and Siplet[2].

The measurement of the acid output following maximal histamine stimulation in patients after gastrectomy or gastroenterostomy does not appear to have been previously studied. The "augmented histamine test", which is based on maximal histamine stimulation, has been shown to "result in an output of hydrochloric acid which is constant for an individual and which represents the maximum parietal cell output of acid" (Kay[3]), and the value of the test is further enhanced by the highly significant correlation which has been shown to exist between the "maximum acid output" and the total number of parietal cells (Marks[10]). The purpose of the present investigation was to determine the "maximum acid output" of the stomach remnant after gastrectomy, and in particular to study the acid output of patients with postgastrectomy or postgastroenterostomy ulcer dyspepsia. These studies will be examined in conjunction with the results of similar tests carried out in patients with intact stomachs (Fig. 1).

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*Awarded second prize in the 1956 Ames Awards Contest.

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The collection of total gastric secretion from the intact stomach is comparatively easy. Continuous suction is applied to a previously screened Levin tube, and the "maximum acid output" is obtained by means of a modification of Kay's[3] augmented histamine test. It was thought, however, that this simple method could not be relied upon to give satisfactory results in patients after Polya-Hofmeister-gastrectomy or gastroenterostomy, because of the possible escape of gastric juice through the stoma and the alkaline reflux from the afferent loop. These difficulties could be overcome if complete blockage of the stoma

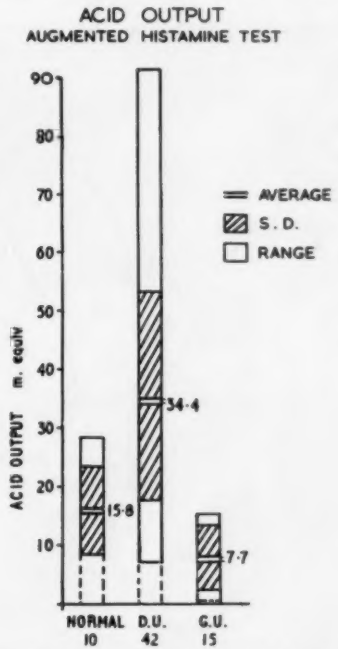

Fig. 1—Diagram showing the "maximum acid output" (posthistamine hour) in different groups of hospital patients.
D.U. = duodenal ulceration. G.U. = gastric ulceration.

were achieved. A dumbbell shaped balloon was therefore devised, and stomal blockage was obtained under radiological control. Total gastric secretion could then be collected by continuous aspiration through a second tube.

Method

A dumbbell-shaped balloon, devised in this Unit, is attached at the lower end of a Levin tube, from the end of which a small weighted bag is suspended (Fig. 2). The patient is intubated after a 12-hour overnight fast, swallowing of

the tube being facilitated by a local anesthetic (Decicaine tablet). The patient is screened radiologically about 1 hour later to ascertain the position of the end of the tube. If it has passed sufficiently far into the efferent loop, the exact site of the stoma is determined by means of a small amount of barium. This is unnecessary in cases where a Friedrich or von Petz clamp has been used for the partial gastrectomy, when the level of the lowest clip gives adequate indication of the stomal site. The tube is then slowly withdrawn until the waist of the slightly inflated balloon is at the stoma; the balloon is inflated with 40 to 50 c.c. of air, and the proximal end of the tube clamped. The adequacy of the stomal blockage is checked by means of a further thin barium swallow. An ordinary Levin tube is then passed into the gastric stump, and the patient is returned to the ward (Figs. 3 and 4).

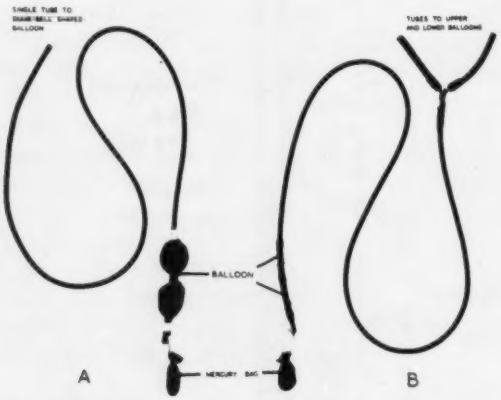

Fig. 2–Stomal blockage balloons.
A: Dumbbell shape used for most of the tests.
B: A later type for easier introduction, developed by Messrs. J. G. Franklin & Sons, Ltd., London, W.1.

The barium-contaminated fasting gastric content is aspirated and the gastric remnant gently washed with warm water to remove the barium. The patient is positioned so as to permit complete emptying of the stomach, usually resting comfortably with one or two pillows (but occasionally propped up at an angle of about 45°) and turned slightly to the left. The remainder of the test follows the standard procedure. Suction is applied continuously, and the "prehistamine secretion" is collected for 1 hour. Anthisan (50 mg. intramuscularly) is given 40 minutes after the commencement of the prehistamine collection. After the injection of histamine acid phosphate (0.04 mg. per kg. body weight subcutaneously), the "posthistamine secretion" is collected for 1 hour. The appearance of bile in the aspirate implies incomplete stomal blockage and may necessitate repetition of the test. The patient is screened at the end of the test to confirm the position of the balloon.

Each specimen of gastric juice is titrated for free and total acidity, Töpfer's reagent and phenolphthalein being used as indicators*. If no free acid is detected throughout the test by means of Töpfer's reagent, the pH is measured electrometrically in each specimen.

The value of this technic was assessed in a group of 14 patients (Table I). Each of these patients was subjected to two histamine tests. The results of continuous aspiration of gastric secretion through a Levin tube, without stomal blockage, were compared with those obtained under conditions of stomal

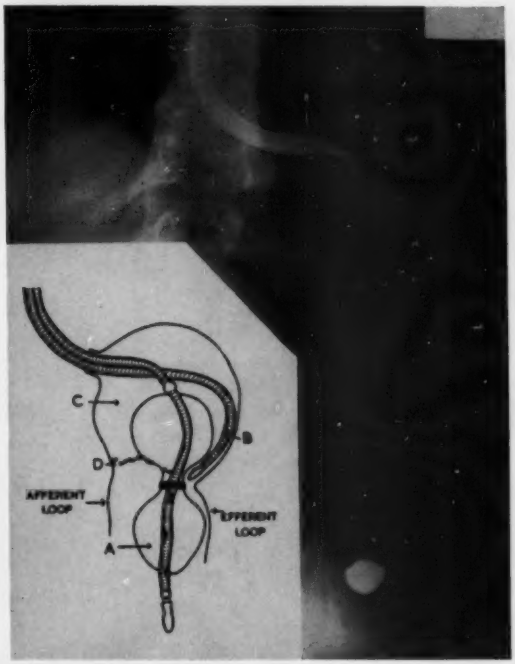

Fig. 3—Showing stomal blockage by dumbbell-shaped balloon (A), with Levin tube (B), in the gastric remnant (C). Metal clips (D).

blockage. The acid output, as determined without stomal blockage, did in fact prove to be a useful measure of the true acid output of the gastric remnant. Satisfactory statistical correlation, however, was found only in those patients with jejunal ulceration or scarring ($0.5 > P > 0.4$). Stomal blockage appeared justifiable, and indeed necessary, in most of the remaining cases ($P = 0.05$).

*The output of acid is determined by multiplying the volume of juice by the acid concentration. The "Maximum acid output" refers to the output of total acid in the "post-histamine secretion", which will also be referred to, in the present paper, as the acid output.

Results

The stomal blockage technic was successfully performed in 29 patients on 37 occasions. Twelve other patients could not be intubated satisfactorily. Four

TABLE I

Comparison of the "Maximum Acid Outputs" Obtained With and Without Stomal Blockage in 14 Patients After Gastrectomy

Case No.	Maximum Acid Output (mEq.)	
	With Stomal Blockage	Without Stomal Blockage
A. Jejunal Ulceration and/or scarring		
14	81.8	72.5
15	32.3	44.2
18	27.2	12.2
20	21.4	20.0
23	16.7	15.1
25	7.7	6.9
14	5.8	4.8
20	1.0	1.1
B. No Jejunal Ulceration or scarring		
8	11.3	11.3
7	10.0	3.8
27	9.0	2.6
6	7.7	5.5
5	7.6	5.4
13	1.3	0.7

Statistical Analysis

		A.	B.
Mean difference (mEq.)		2.14	2.93
S.E. difference (mEq.)		2.75	1.12
	t =	.778	2.62
		0.5>P>0.4	P=0.05

of them had difficulty in swallowing the balloon, while in 3 it failed to pass through the stoma. In 1 patient the lower end of the esophagus would not

permit passage of the balloon. Biliary regurgitation invalidated the test in 4 patients. In 8 patients, with radiologically proven jejunal ulceration, the histamine test was carried out without stomal blockage.

The term "stomal ulceration" will here be restricted to ulceration of the stomal margins. "Jejunal ulceration" will be used to imply ulceration on the jejunal side of the stoma. An ulcer on the gastric side of the stoma will be referred to as "gastric ulceration".

1. Postgastrectomy group:—a. Patients without ulcer symptoms:—(Table II and Fig. 5) The test was carried out on 8 patients, in whom partial gastrectomy for chronic duodenal ulceration had been performed within the previous year. They were all free from symptoms suggestive of possible recurrent ulceration, but half the patients were tested during the first month after operation. In 3

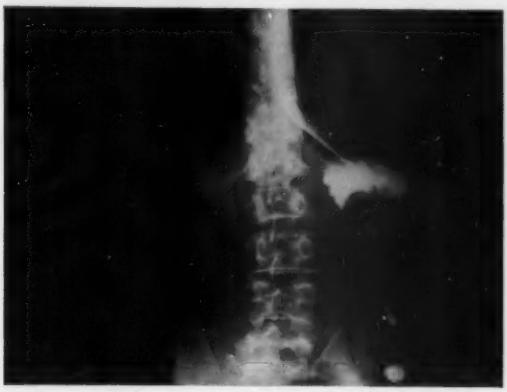

Fig. 4–Showing adequacy of stomal blockage.

patients examined 2 weeks after gastrectomy, the acid output was as high as that produced by the normal intact stomach. The average acid output for the whole group was 12.5± 5.2 mEq HCl/hour, with a range of 7.6 to 20.5 mEq. This suggested that the preoperative acid output was reduced by 50 to 90 per cent within the first year after partial gastrectomy.

Three patients, who underwent partial gastrectomy because of chronic gastric ulceration, had an average acid output of 0.5± 0.2 mEq.

b. Patients with postgastrectomy dyspepsia:—(Table III and Fig. 5) Of 14 patients, in whom ulcer dyspepsia developed after partial gastrectomy, 12 had jejunal ulceration, 1 a gastric ulcer and 1 a "stitch ulcer". The average acid output of the 12 patients with jejunal ulcerations was 28.3±19.8 mEq HCl/hour, the output in 9 of these being of the same order as that in duodenal ulcer patients with intact stomach.

A patient who had undergone two gastrectomies presented a particularly interesting case (Case 14). He was a 35-year old transport driver with a 20-year history of repeated, almost fatal, hematemeses, and of extremely severe ulcer, and postural, dyspepsia. Two other members of his family had ulcer symptoms. A barium meal confirmed the presence of large jejunal ulcers and, in addition, an esophagogastric hiatus hernia (Fig. 6). Irradiation of the gastric mucosa was considered a justifiable alternative to further surgery, which would have involved a third, and preferably total, gastrectomy. After a 1,500 R course of radiotherapy had been applied to the stomach remnant, there was a striking reduction in the enormous acid output of this patient, which was associated with gross irradiation necrosis of the gastric mucosa. Dyspeptic symptoms returned within 6 months, however, and by the end of 9 months the acid output from the gastric remnant had increased to 32 mEq.

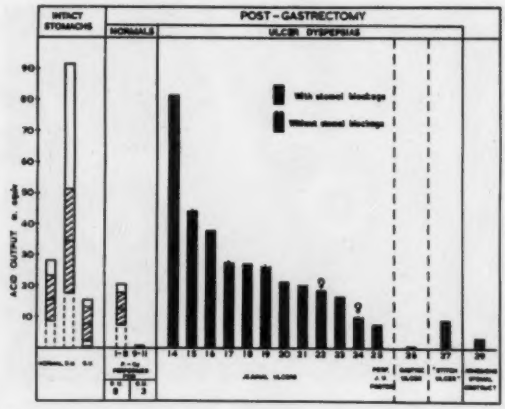

Fig. 5—Diagram showing the "maximum acid output" in different groups of patients after partial gastrectomy.

The association between a very high acid output from the gastric remnant and rapid onset of jejunal ulceration after gastrectomy is illustrated in Case 16. The output of this patient was 38 mEq two months after gastrectomy, and 36 mEq after a further two months. Dyspepsia recurred within 7 weeks of the operation. The acid output before gastrectomy was 91.7 mEq.

Case 25 was that of a patient, with an output of only 7.7 mEq, in whom a perforated jejunal ulcer had been closed only 2 weeks previously. Gastroscopy revealed evidence of gastritis, a possible factor in the comparatively low acid output.

Gastric ulceration was demonstrated both gastroscopically and radiologically in Case 26, a patient in whom gastrectomy had been performed 7 years previously on account of gastric ulceration. This must be very unusual, since

TABLE II

POSTGASTRECTOMY PATIENTS FREE FROM RECURRENT ULCERATION

Case No.	Sex	Age	Acid Output Prior to P/G (mEq. Total Acid in Posthist. Hr.)	Time Since P/G (Years)	Reason for Investigation	X-ray	Acid Output mEq.		Final Diagnosis
							Prehist. Hr. Total Acid	Posthist. Hr. Total Acid	
					Partial Gastrectomy for Duodenal Ulceration				
1	M	46	41.9	2/52	Routine	N.A.D.	2.0	19.5	
2	M	41	40.5	2/52	do.	N.A.D.	4.4	20.5	
3	M	66	36.6	2/52	do.	—	6.8	14.6	
4	M	64	47.0	2/52	do.	—	1.7	8.5	
5	M	52	80.0	6/12	do.	N.A.D.	1.1	7.6	
6	M	37	—	6/12	Mild Dumping	N.A.D.	2.4	7.7	Mild Dumping
7	M	52	59.0	1	Recurrent abd. pain	? def. of stoma from without.	3.4	10.0	Chronic periduodenal infection
8	M	35	40.0	7/12	Mild Dumping	Stoma narrow but otherwise normal	4.0	11.3	Mild Dumping
					Partial Gastrectomy for Gastric Ulceration				
9	F	57	—	3	Postgastrectomy Asthenia Dumping Syndrome	N.A.D.	0.1	0.3	Dumping Syndrome Inadequate Intake
10	M	43	—	3	do.	do.	0.1	0.6	do.
11	M	48	—	3	do.	do.		0.7	do.
					Miscellaneous Group				
12	F	57	—	6	Vague Dyspepsia (Test Repeated)	N.A.D.	1.0 0.3	2.7 2.8	Functional
13	M	61	—	6	Malabsorption Syndrome	do.	1.2	1.3	Chr. Pancreatitis P.G. Malabsorption

P.G.—Postgastrectomy

Swynnerton and Tanner[4] in a large follow-up series, were unable to find any case of proven stomal or gastric ulcer after gastrectomy for gastric ulcer.

In Case 27 partial gastrectomy had been performed one year previously for chronic duodenal ulceration of 7 years' duration. The output of 9 mEq of acid, not unduly high for this type of patient, was considered compatible with, but not strongly suggestive of, a jejunal ulcer. Gastroscopy revealed a "stitch ulcer" on the gastric side of the stoma—a legacy from the partial gastrectomy with a pathogenesis obviously different from that of jejunal ulceration (Fig. 7). A Billroth I conversion was performed for intractable dumping symptoms. The presence of the stitch in the middle of the ulcer was confirmed.

Case 28 was of interest in that the low acid output seemed to be at variance with the radiological diagnosis of a stomal ulcer. Operation revealed a

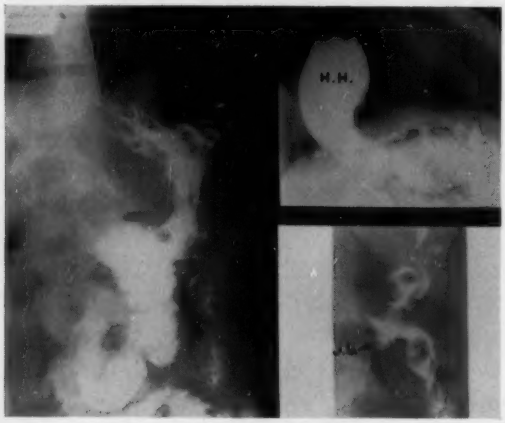

Fig. 6—Case 14, showing jejunal ulceration (J.U.) and hiatus hernia (H.H.).

normal-sized stoma, free from obvious ulceration, but with adhesions in the vicinity.

2. Postgastroenterostomy dyspepsia group:—(Table III and Fig. 8) The dumbbell balloon technic was also employed in measuring the acid output of the stomach after gastroenterostomy, where results obtained by ordinary methods are liable to be vitiated by escape, and afferent loop neutralization, of the gastric contents. The acid output in 4 of the patients in this group was determined without stomal blockage.

In 5 of 6 patients with jejunal ulceration following gastroenterostomy the acid output was very high. One patient, in whom gastroenterostomy had been performed 20 years previously for duodenal ulceration, provided rather anomalous results (Case 34). Gastroscopic evidence of profound gastric atrophy

was in conformity with the extremely low acid output with no free acid, but the presence of an ulcer on the jejunal side of the stoma appeared undoubted. Gross stomal scarring was observed.

Three other patients with postgastroenterostomy dyspepsia, due to gastric ulceration, showed the expected low acid output.

Uropepsinogen studies:—Further evidence of gastric secretory function was obtained by studying the output of uropepsinogen in some of these patients. Sircus[5] drew attention to the value of uropepsinogen estimations as a simple quantitative test of glandular function in the stomach remnant after partial gastrectomy. In his series only those patients with known stomal ulceration had

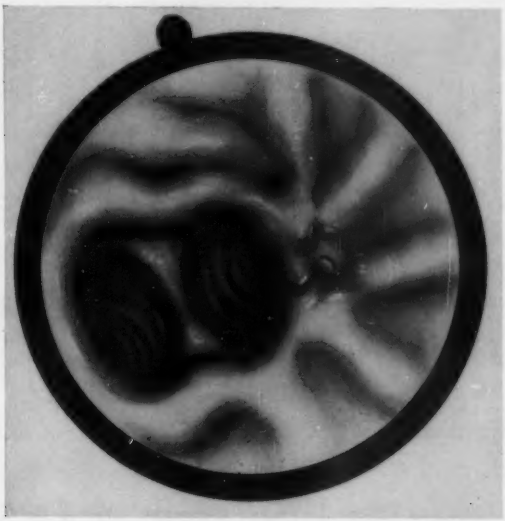

Fig. 7—Gastroscopic impression of "stitch ulcer" on gastric side of stoma (Case 27). The stitch is seen protruding from the base of the ulcer.

a relatively high excretion of uropepsinogen, the remainder of his postgastrectomy group showing little or no output of uropepsinogen. Aitken, Spray and Walker[6] demonstrated a linear relationship not only between the concentration of HCl and that of pepsin in the posthistamine gastric secretion, but also between the concentration of pepsin in the gastric juice and the amount of uropepsinogen excreted in the urine. In the present study uropepsinogen estimations, carried out on 9 patients, failed to show statistical correlation with the maximum acid outputs ($P > 0.1$). All 4 patients with jejunal ulceration and associated high acid output, however, showed a high excretion of uropepsinogen (Table IV).

TABLE III

Postgastrectomy Dyspepsias

Case No.	Sex	Age	Past History		Present History		Investigations				Diagnosis
			Date	Procedures	Date	Symptoms	X-ray	Gastroscopy	Acid Output mEq. Prehist. Hr. Total Acid	Acid Output mEq. Posthist. Hr. Total Acid	
						Jejunal Ulcer Group					
14	M	35	1941 1948 1951 1953 July '55	G/E Attempted Vagotomy P/G Further P/G Gastric Irrad.	June '55 Aug. '55 Dec. '55 Mar. '56 June '56	Ulcer & postural dyspepsia: bleeding Routine do. do. Ulcer & postural dyspepsia	Coarse mucosa J.U. Hiatus hernia J.U. smaller do. do. J.U.	Hypertrophic mucosa	19.8 0.6 0.4 1.5 5.4	81.8 5.8 16.2* 26.1* 32.4*	J.U. Hiatus hernia with peptic esophagitis
15	M	40	1954	P/G	Nov. '55	Ulcer dyspepsia	J.U.		19.8	44.2*	J.U.
16	M	52	Dec.'55 May '56	P/G Vagotomy	Mar. '56 June '56	Mild dyspepsia Routine	J.U.		15.0	38.0 5.4*	J.U.
17	M	56	1930 1934 1954 May '55	G/E G/E "taken down" P/G Vagotomy	Apr. '56 June '56	Ulcer dyspepsia Routine	J.U.		4.0 3.0	27.3* 7.3*	J.U.
18	M	34	1952 Aug. '55	P/G Vagotomy	July '54 Aug. '55 Sept. '55	Ulcer dyspepsia do. Routine	Stomal scarring do. & "stomal ulcer"	Hypertrophic mucosa shrunken stoma do.	 12.4 0.6	22.8 27.2 14.9	J.U.
19	M	26	1954	P/G	Mar. '56	Ulcer dyspepsia	J.U.		2.5	26.4*	J.U.
20	M	49	1949 1951 1953 July '55	Perf. D.U. (1) do. (2) P/G Gastric Irrad.	 June '55 Aug. '55 Apr. '56	 Ulcer dyspepsia Routine do.	 J.U.	 Hypertrophic mucosa Jejunal ulcer	 8.1 0.8 2.6	 21.4 1.0 9.1*	J.U.
21	M	49	1928 1952 Jan. '55	Perf. D.U. P/G Vagotomy	Jan. '55 Feb. '55 May '55	Ulcer dyspepsia Routine do.	J.U., stomal scarring Stomal scarring	N.A.D.	9.8 0.4 0.1	20.1 0.5 0.6	J.U.
22	F	37	1951 1953	Perf. D.U. P/G	1955	Ulcer dyspepsia & bleeding	Jejunitis eff. loop	N.A.D.	1.5	18.8	J.U.
23	M	30	1954 Nov. '55	P/G Gastric Irrad.	Oct. '55 Dec. '55 Apr. '56 June '56	Ulcer dyspepsia Routine do. do.	J.U.		3.6 0.1 0.3 1.9	16.7 1.1 2.3* 5.5*	J.U.

					Apr. '56 June '56	do. do.			0.3 1.9	2.3* 5.5*	
					May '56	Minimal dyspepsia	Scar of J.U.		0.7	10.1*	Healed J.U.
25	M	25	1950 1953 Aug. '55	Perf. D.U. P/G Perf. J.U.	Sept. '55	Routine		Supel. gastritis	0.6	7.7	Postop. gastritis
						GASTRIC ULCER GROUP					
26	M	49	1948	P/G	1954	Ulcer dyspepsia postgastrectomy asthemia Bilious vomiting	G.U.	G.U. Atrophic mucosa	0.6	0.8	G.U.
27	M	32	1948	P/G	1954	Mild ulcer dysp. Dumping syndrome Malabsorption	Stomal ulcer	"Stitch ulcer" on gastric side of stoma Normal mucosa	4.2	9.0	Dumping Syndrome "Stitch ulcer"
						"STOMAL OBSTRUCTION"					
28	M	61	1938 1953	G/E P/G	1955	Vague dyspepsia with vomiting	Narrow stoma "Stomal" ulcer		1.3	3.4	Laparotomy: Stomal adhesions No ulcer seen
						POSTGASTROENTEROSTOMY DYSPEPSIAS—JEJUNAL ULCER GROUP					
29	M	75	1927 Jan. '56	G/E Gastric Irrad.	Dec. '55 Feb. '56 June '56	Ulcer dyspepsia Routine do.	J.U.		3.7 1.3 1.6	60.7* 7.2* 22.1*	J.U.
30	M	49	1938	G/E	1956	Ulcer dyspepsia & bleeding	J.U.		3.9	57.2*	J.U.
31	M	76	1953	G/E	1955	Perf. J.U. & bleeding	J.U.		16.0	55.0	Perf. J.U.
32	M	55	1930	G/E	1955	Ulcer dyspepsia	J.U.	Hypertrophic mucosa	30.0	49.8	J.U.
33	M	61	1938 Feb. '56	G/E Vagotomy	Feb. '56 Mar. '56	Ulcer dyspepsia Routine	J.U.		4.2 0.1	47.7* 2.6*	J.U.
34	M	51	1934	G/E	1954	2 episodes Melena	Stomal scarring	Atrophic gastritis Ulcer on jejunal side of scarred stoma	0.7	1.0	J.U.
						GASTRIC ULCER GROUP					
35	M	49	1932	G/E	1956	Ulcer dyspepsia vomiting	N.A.D.	G.U. (incisma)	2.2	8.1	G.U.
36	F	77	1954	G/E	1955	Ulcer dyspepsia	G.U.		0.2	2.9*	G.U.
37	M	55	1929	G/E	1955	Ulcer dyspepsia	G.U.	Atrophic gastritis antral scarring	0.3	1.0	G.U.

*Test carried out without stomal blockage. G/E—Gastroenterostomy. P/G—Partial Gastrectomy. J.U.—Jejunal Ulcer. G.U.—Gastric Ulcer.

Comment

The inescapable equation of ulcer etiology—acid and pepsin vs. mucosal resistance (Card[7]) allows for certain differences in the pathogenesis of the various types of peptic ulceration. The "acid-pepsin" factor is frequently increased in patients with duodenal ulceration, peptic esophagitis and jejunal ulceration distal to the stoma after partial gastrectomy or gastroenterostomy. The mucosal-resistance factor may be of greater significance in gastric ulceration, which not infrequently occurs in association with an atrophic, or perhaps more expressively, a "sick" mucosa (Fig. 9). The "maximum acid output" in hospital patients who are free from gastrointestinal disease is 15.8 ± 7.4 mEq HCl/hour, the value being slightly greater in young healthy adults. Patients with duodenal ulcera-

TABLE IV

Uropepsinogen Output in Patients After Gastrectomy (P/G) and Gastroenterostomy (G/E)

Case No.	Diagnosis (and previous operation)		Maximum Acid Output mEq. Total Acid	Uropepsinogen u/24 hrs.
14	Jejunal ulcer	P/G	81.8	350
18	Jejunal ulcer	P/G	27.2	850
20	Jejunal ulcer	P/G	21.4	700
21	Jejunal ulcer	P/G	20.1	375
32	Jejunal ulcer	G/E	1.0	75
9	Dumping Syndrome	P/G	0.3	100
10	Dumping Syndrome	P/G	0.6	190
26	Gastric ulcer	P/G	0.8	27
36	Gastric ulcer	G/E	1.0	0

Average normal output (intact stomach) 262 ± 122 (Sircus[5]).

tion have a significantly higher acid output (34.4 ± 16.8 mEq), whereas those with gastric ulceration have a distinctly lower output (7.7 ± 5.4 mEq), (Fig. 1). The acid output obtained under the conditions of maximal histamine stimulation is perhaps the most constant index of gastric secretory function at present available.

Twenty-three of the 37 patients investigated showed evidence of ulceration, 18 having jejunal and 5 having gastric ulceration. Four of the patients with gastric ulceration had a low acid output, associated with atrophic gastritis, whereas the patient with the "stitch ulcer" had a normal acid output and a normal gastric mucosa. Fifteen of the 18 patients with jejunal ulceration had a

very high acid output. In 1 patient (Case 34), however, who appeared to have a chronic ulcer on the jejunal side of the stoma, the acid output was extremely low; it is possible that the mucosa became atrophic subsequent to the development of jejunal ulceration, and that secondary scarring and an impaired vascular supply might have devitalized the region sufficiently to render it liable to further breakdown on an ischemic rather than a primarily peptic basis. It should be remembered that the level of acidity at which peptic activity is reduced to a minimum—pH 5, the proteolytic neutralization point of Hollander[11]—is well

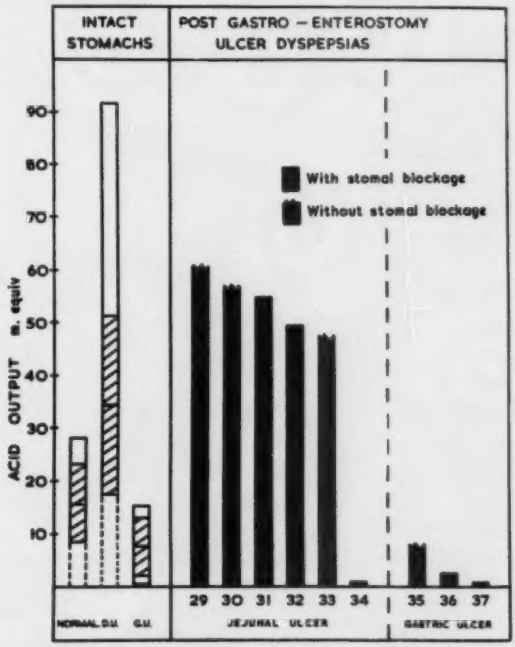

Fig. 8—Diagram showing the "maximum acid output" of patients with postgastroenterostomy dyspepsia.

above the upper level of pH at which Töpfer's reagent indicates the presence of free acid (pH 3.5). Significant acidity may therefore be present despite the absence of free acid, as determined by Töpfer's reagent.

Fourteen of the 37 patients in the series were free from recurrent ulceration. Eight of these patients, investigated within 1 year after gastrectomy for chronic duodenal ulceration, had an average acid output of 12.5 ± 5.2 mEq. The remainder, the majority of whom were operated on for chronic gastric ulceration, had a very low acid output.

Ivy, Grossman and Bachrach[16] regard jejunal ulcer as due principally to the inherently low resistance of jejunal mucosa to acid chyme. The results of the present study indicate strongly the importance of the "acid-pepsin" factor in the pathogenesis of jejunal ulceration. The data also illustrates the significance of a knowledge of the gastric acid output in the elucidation of ulcer dyspepsia following gastrectomy or gastroenterostomy. A high acid output would suggest the possibility of jejunal ulceration, whereas a low value could lend support to a diagnosis of gastric ulceration. The finding of a high acid output after partial gastrectomy, in the absence of symptoms, might indicate an increased liability to jejunal ulceration.

Reports of the occurrence of achlorhydria in about 55 per cent of duodenal ulcer patients following partial gastrectomy (Winkelstein[8], Cornell and Druck-

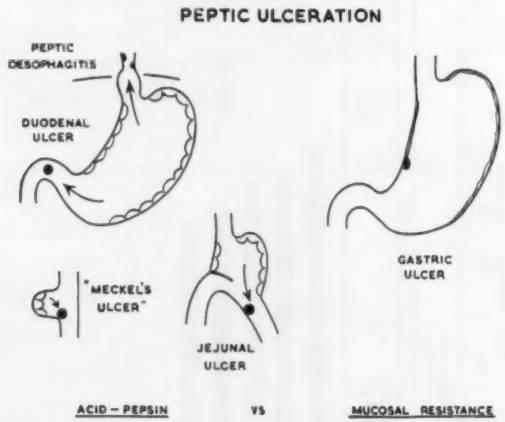

Fig. 9—Diagrammatic representation of factors involved in the various types of peptic ulceration.

erman[15]) may be construed as being at variance with the results of the present study. Similar patients, when tested under conditions of maximal histamine stimulation and stomal blockage, were found to have an acid output of 12.5 ± 5.2 mEq HCl/hour, with free acid invariably present. It is perhaps significant that of 31 patients in Winkelstein's[8] series who were "achlorhydric" with a gruel test meal, 13 showed free acid following gruel and histamine stimulation. The high incidence of achlorhydria previously reported may have been due to the mildness of the secretory stimulus employed, alkaline reflux through the afferent loop, loss of gastric juice through the stoma, or, conceivably, to possible slipping of the end of the Rehfuss tube beyond the gastric remnant resulting in the inadvertent aspiration of intestinal contents. Indeed, the finding of free acid under conditions of the Ewald or Rehfuss test meal may imply the presence of a gastric remnant with a moderate or high "maximum acid output". Shay[1]

holds the view that "no patient should be considered free of the dangers of a marginal (jejunal) ulcer until it can be demonstrated that the gastric contents remains above pH 5," and Cornell and Druckerman[15] reported that proven jejunal ulceration occurred only amongst those patients who had free acid on fractional analysis. These results would therefore appear to be in accord with the finding that jejunal ulceration is frequently associated with a high "maximum acid output" and with the inference that in the absence of symptoms a high acid output might indicate an increased susceptibility to jejunal ulceration.

The cause of the high acid output in patients with jejunal ulceration remains uncertain. It was found that a patient with duodenal ulceration, associated with a very high acid output, may, after an apparently adequate gastrectomy, be left with an acid output exceeding that produced by the normal intact stomach (Case 16). This may suggest failure to remove sufficient of the parietal cell mass in such cases, and casts some doubt on the efficacy of a standardized partial gastrectomy in the treatment of patients with a widely varying acid output. The finding, however, in Case 14, of the enormous acid output of 82 mEq HCl/hour after two gastrectomies would make it unwise, in the present state of our knowledge, to criticize the operation of partial gastrectomy in all patients with high postoperative acid outputs.

It is possible that, in patients such as Case 14, the fault may lie in variations in the physiology of the individual subjects rather than in the particular gastrectomy carried out. The evidence presented suggests that jejunal ulceration following gastrectomy is associated with a high acid output. This high output may be due to an enhanced secretory response from the parietal cells in the gastric remnant, analogous to the possible increase in the "maximum acid output" after the prolonged administration of cortisone; or it may be due simply to a postoperative increase in the number of parietal cells. The latter has been observed as hyperplasia after prolonged histamine stimulation in experimental animals (Cox and Barnes[12], Tongen[9], Cambel and Sgouris[13]), and in young guinea pigs during growth (Marks[14]). It is conceivable that factors, as yet unknown, may be responsible for an increase in the "maximum acid output" and/or an increase in the number of parietal cells, which would account for the high acid output of patients with duodenal ulceration, and that such factors are also fundamental to the production of the high acid output and subsequent jejunal ulceration in a proportion of patients who have undergone partial gastrectomy.

The dumbbell-shaped balloon technic has been a useful stimulus to the study of secretory function of the gastric remnant after gastrectomy or gastroenterostomy. It has proved of value in clinical investigation—in diagnosis, as a guide to treatment, in the postoperative assessment of the success of surgery, and as an index of prognosis in patients after partial gastrectomy. It may find further application as a tool for gastrointestinal research. A carefully performed histamine test without stomal blockage would appear to be adequate in the

presence of jejunal ulceration or scarring. Stomal blockage during the test is preferable in the absence of such ulceration or scarring.

Summary

1. A method of determining the acid gastric secretion after partial gastrectomy or gastroenterostomy is described.

2. The importance of knowledge of the acid output in the investigation of postgastrectomy, or postgastroenterostomy dyspesia is discussed. Jejunal ulceration is frequently associated with an acid output of an order exceeding that found in the normal intact stomach, whereas ulceration of the gastric remnant is associated with a poorly secreting mucosa.

3. Possible factors involved in the causation of the high acid output associated with jejunal ulceration are suggested.

Acknowledgements

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Addendum

The results of a recent investigation carried out by the author since this paper was submitted for publication, offer strong support for the suggestion that the acid output associated with postgastrectomy jejunal ulceration may be due to insufficient reduction of the parietal cell mass in patients with a high preoperative acid output.

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INVESTIGATION OF GASTRIC SECRETORY RESPONSE TO PREDNISONE*

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In investigations of the administration of ACTH and of cortisone to normal subjects over a period of days or weeks, Gray and his coworkers[1-6] found these substances to induce an increase in the basal and nocturnal gastric secretion of hydrochloric acid and pepsin approximating 200 per cent over that of normal levels, and a similar increase in the excretion of uropepsin. They also found that patients under adrenocortical steroid therapy who experienced epigastric distress, or who were developing a peptic ulcer perforation or hemorrhage, developed a coincident peak excretion of uropepsin and an increased gastric acid and pepsin secretion invariably in the ulcer range. They consider the administration of ACTH, cortisone, and hydrocortisone hazardous to patients with peptic ulcer. Their studies suggest that chronic emotional and physical stress stimulate the stomach to secrete increased acid and pepsin by way of a humoral mechanism involving the hypothalamic-pituitary-adrenal axis and independent of the vagus nerves or the gastric antrum.

In view of this postulate and because increased gastric secretion, acidity, and pepsin have been variously implicated as resulting in peptic ulceration, the question arose as to the gastric secretory response to prednisone, the newest of the adrenocortical steroids.

Reports of gastric distress and of the development of peptic ulcer during the administration of prednisone[7-9] made it of particular interest to determine whether or not prednisone evokes a gastric secretory response similar to that supposedly induced by ACTH and cortisone.

Having an opportunity to treat a number of patients with ulcerative colitis, ileitis, and sprue, I undertook a study of gastric secretory responses before and after therapy with prednisone. As individuals with gastrointestinal disorders may differ in response from individuals with a normal gastrointestinal tract, several patients with arthritis were included as controls. The study comprised 14 patients with ulcerative colitis, 2 with regional ileitis, 1 with sprue, and 5 with arthritis.

Method

In each of the 17 patients with gastrointestinal disorders, the volume of gastric secretion and the degree of its acidity (pH) were determined prior to

*Prednisone as Meticorten (T.M.) tablets was furnished by G. Kenneth Hawkins, M.D., Division of Clinical Research, Schering Corporation, Bloomfield, N. J.

TABLE I

GASTRIC SECRETORY RESPONSE TO PREDNISONE

Diagnosis	Duration	Severity	Gastric Secretory Volume and Acidity				
			Before Treatment		After Treatment		
			Volume (c.c.)	pH	Interval	Volume (c.c.)	pH
Ulcerative colitis Rheumatoid arthritis	13 yrs.	severe	10	1	3 mos.	8	3
Ulcerative colitis	11 yrs.	severe	10 mucoid	2	2 wks.	5 mucoid	2
Duodenal ulcer	1 yr.				4 wks.	8 mucoid	2
Ulcerative colitis	8 yrs.	severe	5	2.5	1 mo.	3	3
Ulcerative colitis	6 yrs.	severe	12	2.5	1 mo.	11	2.5
Ulcerative colitis	6 yrs.	severe	5	1.5	1 mo. 4 mos. 7 mos.	5 8 5	2.5 2 2
Ulcerative colitis	3.5 yrs.	severe	8	2.5	3 mos.	10	2.5
Ulcerative colitis Polyposis	3 yrs.	severe	8	2	5 wks.	10	2.5
Ulcerative colitis	1 yr.	severe	3	3	5 mos. 9 mos. 11 mos.	3 mucoid 20 mucoid 10	3.5 3 3
Ulcerative colitis	10 yrs.	moderate	10	1.5	3 mos. 4 mos.	10 10	1.5 1.5
Ulcerative colitis	7 yrs.	moderate	8	1.5	2 wks. 1 mo.	10 12	1 1.5
Ulcerative colitis	6 yrs.	moderate	5 mucoid	2.5	2 mos.	5	2.5
Ulcerative colitis	2 yrs.	moderate	10	1.5	3 wks. 3 mos. 4 mos. 6 mos.	5 20 10 10	3.5 1.5 3 2
Duodenal ulcer							
Ulcerative colitis	9 mos.	moderate	10 mucoid	1.5	2 mos. 3 mos.	8 10	3 3
Ulcerative colitis	6 mos.	moderate	10	2	2 mos.	8	2
Jejunoileitis	16 yrs.	severe	15	2	2 wks. 1 mo.	15 15	2 2
Regional ileitis	5 mos.	moderate	10	2	2 mos.	10	2
Sprue	6 mos.	moderate	15	1.5	2 wks. 1 mo. 2 mos. 5 mos.	5 5 2 5	3 2.5 3 3

therapy. Each patient was given an Ewald test meal when the stomach was empty. After 45 minutes, the gastric secretion was completely aspirated. The volume of gastric juice was measured and its pH determined using Hydrion indicator paper. Two indicator papers were used, one with a pH range of 1 to 2.5 and one with a pH range of 3 to 5.5. The color of the indicator paper wet with gastric juice was compared with colors on a scale from which the pH could be read. The colors in the Hydrion scale are clear and accurate so that variations of 0.5 in pH readings could be accurately determined.

The patients received prednisone in daily dosages of 15 to 30 mg. The duration of administration varied from 1 to 11 months.

The volume of gastric secretion and the degree of acidity were redetermined, using the same technic, after periods of prednisone administration varying from 2 weeks to 11 months.

Results of Gastric Secretory Tests

Table I gives the results of the tests before and after prednisone therapy.

The gastric acidity showed essentially no change in 9 patients. The degree of acidity decreased in 7 patients. In 1 patient, the gastric acidity had increased slightly when the pH was determined after two weeks' treatment with prednisone. The gastric secretion of this patient with ulcerative colitis originally had a pH of 1.5. After two weeks' therapy, the pH was 1.0, but the reading returned to 1.5 at the end of one month of prednisone administration. The volume of the gastric secretion in this patient increased from 8 to 12 c.c. In 3 other patients, minimal increases in gastric secretory volume occurred.

The patients used as controls, 4 with rheumatoid arthritis and 1 with infectious arthritis, received 30 mg. prednisone daily for six months. Before and after prednisone therapy, these patients received a fractional test meal of oatmeal gruel. Rehfuss curves were constructed showing the acidity of the gastric secretion during the two hours following the test meal. Acidity between 40 and 60 clinical units was considered normal. Acidity above 60 clinical units was considered high. The original normal acidity in 4 patients with arthritis remained normal after prednisone therapy. Gastric acidity increased during treatment in 1 control patient, measuring 80 clinical units.

Results of Therapy

Table II gives the results of therapy with prednisone in the 22 patients in this study.

Ulcerative colitis:—Complete healing of ulcerative colitis lesions took place in 1 patient treated for three months with 15 mg. prednisone daily. Major improvement occurred within two months in another patient who received a sim-

ilar dosage. Nine patients improved moderately when 30 mg. prednisone daily were administered for one to seven months. In one of them, the initial daily dosage of 30 mg., which was administered for eight months, could be reduced to 15 mg. Treatment was continued for an additional three months with this amount. Only slight improvement occurred in 3 other patients during treatment for two, three, and six months, respectively.

Two of the patients with ulcerative colitis also had an active duodenal ulcer proved by roentgenographic examination. Prednisone administration caused no

TABLE II

RESULTS OF THERAPY WITH PREDNISONE

Diagnosis	No. Pts.	Daily Dosage (mg.)	Duration (mos.)	Degree of Improvement				
				Complete Healing	Major	Moderate	Slight	Little or None
Infectious arthritis	1	30	6			1		
Rheumatoid arthritis	4	30	6			4		
Ulcerative colitis	14	30	8			1		
		15	3					
		30	7			1		
		30	3					
		15	3				1	
		30	3			2	1	
		30	2				1	
		30	5 wks.			1		
		30	1			3		
		15	3	1				
		15	2		1	1		
Regional ileitis	2	30	2	1				
		30	1					1
Sprue	1	30	5			1		

exacerbation of ulcer symptoms. One of these patients received 15 mg. daily for two months and the other 30 mg. daily for three months and 15 mg. daily for a second three-month period.

Sprue:—The patient with sprue received 30 mg. prednisone daily for five months. Diarrhea disappeared and the patient gained weight.

Regional ileitis:—Moderately severe regional ileitis in 1 patient healed completely during treatment for two months with 30 mg. prednisone daily. Severe

jejunoileitis of 16 years' duration in 1 patient showed little improvement after treatment for a month with 30 mg. daily.

Arthritis:—Rheumatoid arthritis in 4 patients and infectious arthritis in 1 patient responded well to prednisone therapy. These 5 patients improved moderately during treatment for six months with daily dosages of 30 mg.

Summary

Twenty-two patients with ulcerative colitis, sprue, ileitis, and rheumatoid or infectious arthritis were treated with 15 to 30 mg. prednisone daily for periods of 1 to 11 months. Gastric secretion measured before and after prednisone therapy showed a decrease or essentially no change in volume or acidity in 20 patients. In 1 patient with ulcerative colitis, a minimal increase in volume and acidity occurred. One month after beginning therapy in this patient, the pH of the gastric secretion had returned to the pretreatment level. Among 5 patients with arthritis serving as controls, the gastric acidity increased in only 1 during the administration of prednisone.

These results indicate that prednisone does not significantly increase gastric secretory volume or acidity. No exacerbation of ulcer symptoms occurred during the administration of prednisone to 2 patients with active duodenal ulcers.

Eleven patients with ulcerative colitis, 1 patient with sprue, 1 patient with regional ileitis, and 5 with rheumatoid or infectious arthritis improved during treatment with prednisone. Jejunoileitis in 1 patient showed little response and only slight improvement took place in 3 patients with ulcerative colitis.

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EVALUATION OF MEDICAL TREATMENT OF GASTRODUODENAL ULCER IN THE NEAR AND MIDDLE EAST

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Ulcogenesis

Ulcer is a general and local disease—local manifested by the ulcer lesion, and general due to reflection on the stomach and duodenum of a sustained emotional, psychical and physical stress which gives rise to functional physiologic and biochemical alterations. This reflection is conveyed to the stomach and duodenum by two independent pathways: nervous and endocrinous. The nervous is transmitted to the stomach and duodenum through the vagus nerve whose ramifications and nerve endings are profusely dispersed in the walls of both organs especially the small curvature of the stomach. It is to be remembered that the vagus nerve arises from the side of the medulla oblongata and its function concerns motion and sensation. Stimulation of vagus centers is carried along the course of fiber tracts which proceed from the anterior hypothalamus. The endocrinous is mediated through the pituitary and adrenal glands which are the most concerned of the endocrine system.

Emotional (fear, anxiety, worry, etc.) and physical (exertion, fatigue, surmenage, abrupt changes of temperature, etc.) stress initiated in the cerebral cortex, probably in the frontal lobes, influence the hypothalamus through neural and/or chemical paths. From the hypothalamus impulses stimulate the pituitary to release adrenocorticotrophic hormone which in turn activates the adrenal cortex to release a number of steroid hormones. These adrenal hormones stimulate gastric glands to secrete an abundant increased output of gastric secretion.

Combination of these two factors, namely, the vagal and hormonal is, indubitably, basic in the formation of ulcer. The vagal plays a primary role on motion, producing *vagotony*, the hormonal on secretion. We believe, however, that both factors are insufficient to cause an ulcer unless the constitutional factor which predisposes to ulcerous disease is present.

Ulcer in the Near and Middle East is on progressive increase. It is interesting to give herewith a sketch of the information I have collected for my recent book "Gastroduodenal Ulcer and Cancer"[8], from the Arab countries of the Near and Middle East.

Lebanon:—In the statistics of the French Institute of Radiology, School of Medicine in Beirut, of 2,000 cases submitted to exploration for ulcer, Ponthus found the following: Gastric ulcer, 59; ulcer of pyloric region, 65; duodenal ulcer, 579; gastric cancer, 30; gastroduodenitis, 246; no lesion, 1,021. Also he confirms that ulcer is on the increase.

Egypt:—Azmi Pasha finds duodenal ulcer very common and on the increase and gastric ulcer very rare.

Iraq:—According to El-Badri, ulcer is not frequent and the proportion of gastric ulcer to duodenal is 1 to 1.3.

Syria:—Khater reports that 60 per cent of ulcers are duodenal and 40 per cent are gastric, or a proportion of 3 to 2, in other words a slight difference between the two localities.

Arabia:—Harrison does not notice any increase of duodenal ulcer and the proportion is 12 duodenal to 2 gastric ulcers.

It is of no less interest to note that ulcer is observed frequently and is on the increase among Aramco people who proceed from the United States to Saudi Arabia. The cause is not clear. Is the climate to be accused, or the environment? Certainly we cannot attribute it to food because most of the food consumed is imported directly from home. Nor can excess of alcohol be incriminated. Saudi Arabia is a dry state and alcohol consumption of any kind is strictly prohibited under severe penalty. And the least it can be due to is financial worries as salaries surpass the desired guarantee.

Comments

Nothing until now, proves to be specific and definite in the treatment of gastroduodenal ulcer. This is obvious and logical, because as long as the exact etiology of ulcer is unknown and believed to be multiple, therapeutics will eventually continue to be nonspecific and multiple.

Long experience, failures and successes, in the management of ulcer disease lead us to the admission of the following facts:

Basic treatment of ulcer is medical and not surgical.

Basic treatment of ulcer complications is surgical and not medical.

Medical treatment of ulcer is ambulatory.

Medical treatment of ulcer complications is hospitalization.

Medical treatment should be guided by the tolerance of the patient.

Strict diet, bland diet, and straight milk diet in noncomplicated ulcer are unnecessary[2].

Early in 1938 in a general session dedicated to gastroduodenal ulcer by the Mexican Chapter of the American National Gastroenterological Association, now the American College of Gastroenterology, I communicated the following opinion to which I still adhere despite pessimistic exaggeration in some of its contents:

"Gastroduodenal ulcer is the problem of digestive pathology which leads many a time to confusion. While its etiology is obscure, its diagnosis is not so easy. Asymptomatic duodenal ulcer is frequent, a fact known since Moynihan. Roentgenology demands a large experience, special technic and the cooperation of the clinician and the surgeon. Gastric chemistry is a poor help due to the oscillation of the findings. Radical cure, unfortunately, does not exist, not even a permanent relief on a large percentage of cases, because relapses and recurrences of the apparently and clinically healed ulcer are common, as well as, the appearance of ulcer on the stoma after a gastroenterostomy or a gastrectomy. Prognosis is reserved because we have no means of being absolutely sure of a definite cure, and, even when roentgenology registers total disappearance of any direct or indirect sign of the lesion, yet it is subject to a flare-up any time.

"I am glad to say that the tendency of the surgeons in our Association has been lately conservative, shifting towards the restriction of intervention limiting it to complications only.

"I, personally believe that treatment of ulcer is essentially and basically medical. Surgeons are very enthusiastic over the results they report. Their routine is to operate frequently without severe selection of appropriate cases. We physicians should protest against this practice and insist that the surgeons choose, with closer study, their candidates. I do not mean by this to ignore, or minimize in the least, the valuable help that they render us. I only want to beseech them to reduce, to the minimum possible, the profuse interventions and to operate only when the operation is the last resort. The reason for this is obvious. Remote results of the operated patients are not very satisfactory, but rather generally palliative due to the flare-up of symptoms. A considerable number of them are obliged to consult the physician and follow the treatment for even years, and perhaps, for life time."

Martin of Johns Hopkins expressed the following: "It is not too much to hope that the day will come when we will regard peptic ulcer as a disease whose treatment is medical, when we shall look upon the patient who requires surgery, not as one who has failed to respond to medical treatment, but as one who has not received adequate sympathetic and understanding attention[4]."

We are convinced that ulcer treatment is the domain of the physician. Although 50 per cent of the cases are cured or definitely relieved by surgical intervention, a large percentage of the operated are forced to go back, sooner or later, to the physician.

The aim of medical treatment should be to relieve complaints, heal lesion and prevent relapse or formation of new ulcer[9].

As the underlying factor of ulcer diathesis is vagotonia, and as psychical emotions influence vagal functions and thus contribute largely to the appearance,

as well as the recurrence of ulcer, treatment should be directed primarily against these front lines.

Antivagotonic Drugs

Antispasmodics so far in current use, such as belladona and its derivatives, possess a more or less cholinergic blocking action, that is to say, they are as well anticholinergic. All the preparations in vogue influence HCl acid output and gastroduodenal motility. The advantage of the new anticholinergic drugs (Banthine, Pro-Banthine, Prantal, Antrenyl, etc.) is claimed to be in that the side-effects are minimal or nil. Yet, in our experience we could not elicit a great

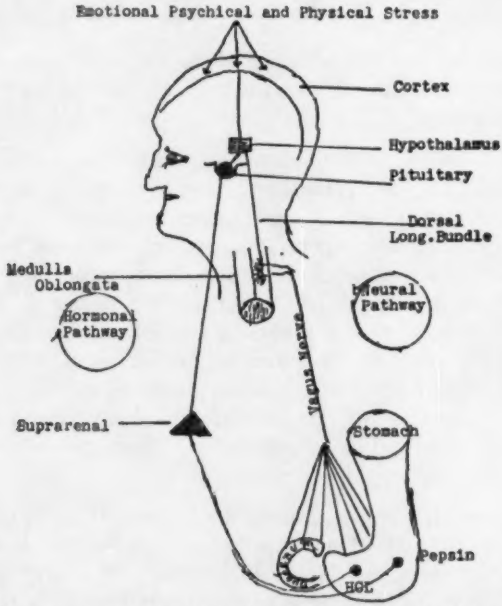

Fig. 1—Diagram showing neural and hormonal pathways contributory to gastroduodenal ulcer formation.

difference between the old and new groups. Intolerant, idiosyncratic or allergic patients complained (more or less) of side-effects when using either preparation of the two groups. Patients, whose chief complaint was pain, benefited more immediately by the new anticholinergics. It seems that they possess a specific action on the element pain. A comparative study of these drugs shows that Pro-Banthine is much stronger, less toxic and has less side-effects than Banthine. It is as well much more effective as an anticholinergic than atropine and acts more on vagal terminals. To Prantal is attributed more therapeutic effectiveness and less side-effects; it may be the most promising drug (Marks[3]). Prantal and

Antrenyl gave, in our hands in some cases who suffered intractable pain, miraculous immediate results. These new drugs should not be used in cases of gastric dilatation, pyloric functional or organic obstruction, prostate enlargement and glaucoma (Nasio[5]).

Belladona and its derivatives (atropine, hyoscyamus) still resist renovation and modernization. We are faithful adherents to their use. They should be given until physiologic effect is attained otherwise results are poor, discouraging and action reversible. They rather increase trouble when administered in insufficient doses.

Transmission of any impulse is conducted chemically and electrically: chemically through acetylcholine and electrically through nerve supply. Atropine blocks vagal nerve endings but does not paralyze them and thus prevents acetylcholine from acting on tissue cells and consequently diminishes motor activity and emotional stimuli (S. Wright[10]).

As to the administration of atropine intravenously, we honestly confess that the remote result of this method is far from being encouraging or necessary. It is not worth the trouble and the risk. It should be limited to selected cases, but not employed routinely. We are convinced that if atropine works well in a certain case it can do so even if administered per os. Moreover, preserve the veins of your ulcer patients. You do not know when you will be called to use them.

Hyoscyamus has an action identical to belladona. The hyoscine it contains is a fairly good cerebral sedative. We are fond of the following formula:

Tinct. of Belladona

Tinct. of Hyoscyamus $\overline{aa}$ 20 c.c.

to be taken 20 drops in water before meals or 10 drops before and after meals. We generally add:

Kaolin (pure)	0.30
Sodium bicarbonate	0.15
Bismuth or Calcium Carbonate	0.20

for one cachet to be taken half an hour to an hour after meals and when necessary.

Phenobarbital (luminal), profusely used to calm irritation of central nervous system, should be administered with caution because of its toxicity and habit formation.

Licorice or root of glycyrrhiza (sweet root) preparations (Rabro, SucMac, Phytol-A, Caved-S, etc.) contain the juice of the roots deprived of their nocive

active principle acid "glycyrrhizine". Licorice has been used for a long time by the public as chewing gum and in the Near East as one of the popular refreshment drinks. Its beneficial action on digestive organs was discovered by chance, as it is the case with many remedies, not so long ago in Holland. Licorice preparations proved to be active antacids, antispasmodics and good protectors of the mucosa. It is claimed to have substances that possess hormonal action (antihistaminic, anticholinergic). In this connection, it is opportune to mention the fact that antihistaminic drugs have no action on gastric secretions. Moreover, it is believed that licorice stimulates circulation in damaged ulcerous regions of the mucosa. Its laxative effect is most welcome because the majority of ulcer patients suffer constipation. It goes without saying that licorice gives the stools

TABLE I

	Cases	Sex	Age	Relief	Healing
Banthine Pro-Banthine	55	35 M. 20 F.	17-20	25	6
Prantal	45	30 M. 15 F.	15-53	15	3
Antrenyl	42	30 M. 12 F.	20-60	13	4
Rabro	88	70 M. 18 F.	25-50	45	15
Belladona and Derivatives	95	70 M. 25 F.	10-70	60	18
	325	235 M. 90 F.	17-58	158	46

a dark color and above all it is nontoxic and has no side-effects (Nelemens, Stamperius, Revers[6]).

It is to be noted that antacids are usually prescribed along with these preparations. Bismuth, the traditional king of the alkalis, given in massive doses should be abandoned. Almost all so-called modern preparations contain small doses of bismuth, calcium and sodium bicarbonate.

Case Reports

An appraisal of the clinical results of these antivagotonic drugs on 325 ulcer patients seen and treated by us in the last few years is indicated in Table I. Seventy per cent of these cases are Lebanese, the rest belong to the other Arab countries of the Near and Middle East.

With the new anticholinergic preparations, 37 per cent of the cases were relieved of symptoms and 9 per cent were cured; with Rabro 50 per cent were symptom-free and 17 per cent cured; with belladona and derivatives 60 per cent were relieved and 19.5 per cent healed. Thus out of the 325 cases treated, 158 became symptom-free and 46 cured, or 49 per cent relieved and 14 per cent healed. The cured cases include only those whom we were able to control by roentgenologic check-up. Unfortunately only 62 per cent of the patients could be followed-up.

It seems that these agents possess an elective action upon ulcer, because when one drug failed, another replaced it with amazingly good response. This proves the individual personality of ulcer patients, as well as the individual personality of each ulcer.

Seventy per cent of the 325 cases have more than two members of immediate family, and 15 per cent of distant relatives, who suffered ulcer disease. It is striking to note that location in each family was the same—either duodenal or gastric. Fifteen per cent suffered hepatoenteropathy, and 30 per cent smoked and drank.

Summary

The incidence of ulcer disease in the Near and Middle East is on the increase. The cause of ulcer is attributed to vagotony and psychical emotions. Ulcer treatment is considered to be the domain of the physician. An evaluation of the comparative clinical results obtained with the old and new antivagotonic drugs, in 325 cases, is detailed.

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President's Message

Our Public Relations Policy

Some doctors have distorted ideas as to the meaning of "Public Relations". Actually the doctor is the only adequate public relations agent in medicine. Therefore, if he is to be effective in public relations, he must understand it and be sold on its value himself.

As individuals we can sell our ideals and objectives to others by taking time out to explain what field we cover in medicine and why we are not in conflict with any other organization in gastroenterology. We must be modest in our explanations and sincere in our discussions. In this way the college will gain stature and the respect of all doctors. Misunderstanding of our motives must be eliminated and each and every one of us must dedicate himself to the elucidation of our objectives. Such clarification is necessary locally, statewide and nationally.

We should cooperate with other organizations. We must assert leadership no matter where we are or where we live. We must publicize gastroenterology whenever the opportunity presents itself. This can be aided by encouraging financial grants and research in our field. We should aid in developing departments of gastroenterology in clinics, hospitals and medical schools. Postgraduate courses and training should be sponsored and continued. We must not decline optional chance appearances at medical meetings, or on radio or television programs if requested by a duly approved medical group.

Our wives are members of various county and state Auxiliaries. They too could be effective public relations agents by publicizing the college among their colleagues.

We must agree, we are the public relation agents of our own American College of Gastroenterology. Let us not fail in our responsibilities.

Arthur A. Kirchner

NEWS NOTES

Course in Postgraduate Gastroenterology

The American College of Gastroenterology announces that its Annual Course in Postgraduate Gastroenterology will be given at The Somerset in Boston, Mass. on 24, 25, 26 October 1957.

The Course will again be under the direction and co-chairmanship of Dr. Owen H. Wangensteen, Professor of Surgery of the University of Minnesota Medical School, who will serve as surgical co-ordinator and Dr. I. Snapper, Director of Medical Education, Beth-El Hospital, Brooklyn, N. Y., who will serve as medical co-ordinator. Drs. Wangensteen and Snapper will be assisted by a distinguished faculty selected from the medical schools in the Boston area.

The subject matter to be covered in the Course, from a medical as well as surgical viewpoint, will be, essentially, the advances in diagnosis and treatment of gastrointestinal diseases and a comprehensive discussion of diseases of the mouth, esophagus, stomach, pancreas, spleen, liver and gallbladder, colon and rectum, with special studies of radiology and gastroscopy.

For further information and enrollment write to the American College of Gastroenterology, 33 West 60th Street, New York 23, N. Y.

Fifth International Congress of Internal Medicine

The International Society of Internal Medicine has announced that its Fifth International Congress of Internal Medicine will be held at the new Sheraton Hotel, Philadelphia, Pa., 24-26 April 1958. This will be the first meeting of the Society outside of Europe. In making the announcement, the International Society's President, Sir Russell Brain, who is also President of the Royal College of Physicians of London, said, "The Executive Committee of the Society has chosen the United States for its Fifth Congress in response to an invitation extended by the American College of Physicians and with the objective of securing greater American participation in its deliberations and of allowing foreign members, at first hand, to learn more about American developments in the medical sciences".

At the Philadelphia Congress it is planned, through lectures and panels, to analyze medical achievements of world-wide significance, to evaluate certain apparent problems and to chart courses of action designed to enhance technical knowledge and to aid in the continuing war against disease. At the same time, the plan inlcudes such social and cultural activities as will tend to promote cooperation, friendship and mutual understanding among physicians and peace among their countries.

ABSTRACTS FOR GASTROENTEROLOGISTS

GASTROINTESTINAL TRACT

A COMPARATIVE STUDY OF THREE ANTICHOLINERGIC DRUGS—MONODRAL, PAMINE AND PRO-BANTHINE: Richard D. McKenna, Robert H. Bourne and Eva Arendt. Canad. M. A. J., 74:685 (1 May), 1956.

In this study, the following three drugs were evaluated: Monodral, Pamine and Pro-Banthine on proven peptic ulcer cases. Also Pro-Banthine in suppository form was evaluated to find a long acting drug useful in suppressing nocturnal gastric secretion.

Monodral has greater results in suppressing acidity and raising pH than the other two drugs, has a longer duration of action, anacidity tending to persist 2 and ¾ hours after a single dose of 10 mg. and in several cases up to 3 and ¾ hours.

Pamine had little effect in suppressing gastric acidity or secretion volume on a single dose of 5-7.5 mg. To approach the effect that 10 mg. of Monodral produced, up to 20 mg. of Pamine had to be used.

A single dose of 30 mg. of Pro-Banthine reduced secretion volume 76 per cent and acidity 40 per cent. No further improvement was obtained with 45 mg. Using 25 mg. suppositories acidity was reduced 60 per cent but with 50 mg. reduction was 100 per cent. A combination of the rectal and oral caused a more prolonged and profound effect than either used alone. Side-effects were few in number and less with Monodral and Pamine.

LOUIS K. MORGANSTEIN

ADENOMATOUS POLYP OF DESCENDING PORTION OF DUODENUM SIMULATING BLEEDING PEPTIC ULCER: Arnold Gottesman. J. Internat. Coll. Surgeons, 25:562 (May), 1956.

Benign polyp of the duodenum, a comparatively rare clinical indentity, giving no characteristic symptoms of its presence is usually discovered during routine x-ray examination or at laparotomy for some other condition.

Preoperative x-ray studies showed a filling defect in the descending portion of the duodenum, diagnosed as polyp or scar from healed duodenal ulcer.

At operation a specimen 1.3 x 1.2 x 0.7 cm. was removed from the second portion

of the duodenal wall, which histologically showed polypoid formation, covered with glandular epithelium and hemorrhage in the underlying stroma, benign polyp.

The possible neoplastic formations at this site are polyp, fibromyoma, adenoma, endothelioma, hemangioma and fibroma.

J. EDWARD BROWN

INTESTINES

IDIOPATHIC CHRONIC ULCERATIVE COLITIS AND REGIONAL ENTEROCOLITIS: A. J. French and S. A. Vander. Am. J. Roentgenol. 74:977 (Dec.), 1955.

Fifty-three cases of idiopathic chronic ulcerative colitis and 30 cases of regional enterocolitis are reviewed. The average age of onset was six years less in ulcerative colitis than in regional enterocolitis. Most cases of ulcerative colitis involved the colon alone, but the ileum was involved in 14 cases, and the colon other than the rectum in 12 cases. The exudative inflammatory process seen in idiopathic chronic ulcerative colitis and the productive inflammation which characterizes regional enterocolitis usually permit separation of these conditions from each other and from other inflammatory processes. Idiopathic chronic ulcerative colitis and regional enterocolitis are clinicopathologic and roentgenologic entities which in most instances are readily distinguishable. The etiology and pathogenesis are not established, but tissue hypersensitivity reactions may account for the chronicity of the processes. Pseudotubercle formation, metaplasia of intestinal epithelium to Brunner's type glands, and barium granulomas may be encountered. Carcinomatous changes occurred in 3.8 per cent in ulcerative colitis; it was not found in regional enterocolitis.

FRANZ J. LUST

ROENTGEN FINDINGS IN REGIONAL ENTERITIS: R. H. Marshak and B. S. Wolf. Am. J. Roentgenol. 74:1000 (Dec), 1955.

The most common nonspecific inflammatory lesion of the small intestine is regional enteritis. It may affect any portion of the small intestine, however, it most commonly involves the terminal ileum. Since stenosis is such a prominent feature of the disease the roentgen findings have been conveniently divided into the nonstenotic and stenotic stages. The roentgen changes from the earliest alterations to the late stenotic stage as well as the changes characteristic of the site of involvement are described. The length of involvement is usually determined on the initial examination. Proximal and distal extension without operation is uncommon. The large majority of cases demonstrate the disease to be progressive. However, many years may elapse before stenosis supervenes. Resolution is infrequent. Regional ileitis extending into the colon is uncommon in the authors' experience. Recurrent ileitis following side-tracking procedures with and without resection of the diseased bowel occurs with disturbing frequency. Again, the new terminal ileum is involved without involvement of the colon. The combination of regional enteritis and right-sided ulcerative colitis was seen 20 times in this series of cases. Diffuse ulcerative colitis with regional ileitis was uncommon without previous operative intervention. Nonspecific ulcerative colitis may involve the distal portion of ileum, and the small intestinal lesion must then be differentiated from regional enteritis and specific inflammations of the small intestine which can be recognized on the roentgen examination in this area.

FRANZ J. LUST

CHRONIC ULCERATIVE COLITIS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: Charles H. Brown, John R. Haserick and Earl K. Shirey. Cleveland Clin. Quart. 23:43 (Jan.), 1956.

The simultaneous occurrence of chronic ulcerative colitis and systemic *lupus erythematosus* seem to be exceedingly rare. There is considerable evidence that chronic

ulcerative colitis may be a systematic connective tissue (collagen) disease, rather than solely a localized mucosal infection, pathologically similar to systemic *lupus erythematosus*. Such a relationship is indicated by simultaneous appearance of chronic ulcerative colitis and such symptom-complexes as: erythema nodosum, rheumatoid arthritis, iritis, and glomerulitis with greater than chance frequency.

Treatment consisted of hydrocortisone (20 mg. b.i.d.), chloroquine, Azulfidine, Pyrodoxine, and Isoniazid. Stools were reduced to 4 a day in two weeks, but the joints continued painful. By July the arthritis had improved but it was necessary to discontinue the Azulfidine.

REGINALD B. WEILER

LIVER AND BILIARY TRACT

ROENTGENOGRAPHIC OPACITY OF THE HEPATIC CIRCULATION: Alejandro Celis, M. E. Villalobos, H. del Castillo and Jorge F. Espinosa. Am. J. Roentgenol. 74:1089 (Dec.), 1955.

A new method for the roentgenological study of the liver is described by means of the injection of a radiopaque substance into the suprahepatic veins. The authors use from 15 to 30 c.c. of a 70-80 per cent nosylan solution injected as rapidly as possible. The visualization of the suprahepatic system and of the parenchyma of the catherized lobule is made possible. The opaque substance enters the portal vessels against the portal blood flow. Subsequent studies will be necessary to judge the value of the procedure. The catherization of the suprahepatic veins and the injection of the opaque substance have proved harmless to the patient and to the liver in the thirty cases studied.

FRANZ J. LUST

COMPARISON OF CLINICAL DIAGNOSIS IN LIVER DISEASE WITH CHEMICAL AND BIOPSY FINDINGS: J. P. Andrews. North Carolina M. J. 17:14 (Jan.), 1956.

Again the general value of a liver biopsy is corroborated especially when a battery of chemical tests fails to lead to a definite diagnosis. While the supplemental value of the needle liver biopsy is inferred in the article, the authors believe that it is "by far the most accurate (single) diagnostic tool".

Not stressed, however, is that there is always a small but definite risk of complications by the procedure itself and that a pathologist experienced in interpreting the slides is a *sine qua non*.

Therefore, it still behooves us to run chemical tests first and use the liver biopsy only when a diagnosis cannot be made by the clinical and laboratory data readily available.

A. M. SUSINNO

PATHOLOGY AND LABORATORY RESEARCH

SUPPRESSION OF GASTRIC HYDROCHLORIC ACID SECRETION BY ENZYME INHIBITORS: Franklin Hollander and Henry D. Janowitz. A.M.A. Arch. Int. Med. 97:194 (Feb.), 1956.

Two groups of chemicals reducing gastric acidity are administered for the treatment of peptic ulcer: those which neutralize hydrochloric acid already secreted into the gastric lumen and those which block the nerve stimulation of acid formation either by inhibiting the ganglia or the postganglionic fibers. There is a third group of substances that may inhibit gastric acidity by blocking the enzyme systems necessary for the intracellular elaboration of hydrochloric acid. Many inhibitors are available for animal experiments but they are unfortunately too toxic for human use. So far only Diamox can be applied intravenously in large doses (60 mg./kg. body weight) for the blocking of carbonic acid anhydrase. This drug is harmless but the large dosage required is impractical. Nevertheless, new enzyme inhibitors are being synthesized that may be better suitable for human use.

H. B. EISENSTADT

BOOK REVIEWS FOR GASTROENTEROLOGISTS

1955-56 YEAR BOOK OF ENDOCRINOLOGY: Edited by Gilbert S. Gordan, M.D., Ph.D., Department of Medicine, University School of Medicine, etc., etc., San Francisco, Calif. 367 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill. Price $6.00.

As in previous years, subjects relating to endocrinology are abstracted from medical journals throughout the world. Among more recent studies (page 298), the reader will find a special article dealing with the hypoglycemic action of sulfonamides in diabetes mellitus, its effectiveness orally. It is recommended that general practitioners and all other physicians should familiarize themselves with this preparation before prescribing it. Another instructive chapter (page 339) deals with endocrine treatment of neoplastic diseases.

An adequate cross and author's index adds to the value of this volume.

THE OFFICE ASSISTANT IN MEDICAL OR DENTAL PRACTICE: Portia M. Frederick, Instructor, Medical Office Assisting, Long Beach City College and Carol Towner, Executive Assistant, Department of Public Relations, American Medical Association. 351 pages, illustrated. W. B. Saunders Company, Philadelphia, Pa., 1956. Price $4.75.

After reading this interesting and instructive book, the reviewer finds that he has learned a great deal about the training, management and efficiency of office personnel.

A very important and costly item is the hypodermic syringe. Careless handling of syringes result in unnecessary expenditure and the doctor as well as his assistant will greatly profit by reading page 241, "Care of syringes". This alone is worth the price of the book. Many other useful hints and instructions enhance the value of "The Office Assistant" and it is highly recommended as necessary for the smoother and more efficient administration of the office.

ANNUAL REVIEW OF MEDICINE—VOL. 7: David A. Rytand, Editor, Stanford University School of Medicine, and William Creger, Associate Editor, Stanford University School of Medicine. 611 pages, illustrated. Annual Reviews, Inc., Stanford, Calif., 1956. Price $7.00.

The volume is divided into 22 chapters and covers the entire field of medicine, including laboratory aids, cardiology, gastroenterology, psychiatry, endocrinology, nutrition and others. At the end of each chapter, a well chosen review of the literature is appended.

On page 159, laboratory aids to diagnosis and therapy, brings to the attention of the physician the latest findings in malignant carcinoid, the elevated concentration of 5-hydroxytryptamine (serotonin) in blood. The presence of increased concentrations of this substance provides a diagnostic comparable to the measurement of acid phosphatase in prostatic carcinoma, adrenalin and nonadrenalin in pheocromocytoma or of gonadrotropin in chronic epithelioma. Further diagnostic nuggets deal with diagnosis of pancreatic disease, especially elevated serum amylase in acute pancreatitis. The administration of opiates, anuria, strangulation of the intestine, perforation of a peptic ulcer and laboratory errors, may cause elevated serum amylase. Antithrombin titer may be substituted for the secretin test and is graded second in usefulness when the secretin test could not be performed. Other tests deal with calcium and phosphate, electrophoresis and proteins, lipoproteins and lipids, blood ammonia, especially in hepatic coma, enzyme activity of body fluids.

In diseases of the gastrointestinal tract (page 309), the reader will find many of the more recent observations, such as the rate of absorption of water from the stomach and small bowel in human beings. It is interesting to note that in the stomach, 67 per cent of the water was absorbed in 34 minutes and 95 per cent in 54 minutes, while from the small bowel, the absorp-

tion was much faster, 67 per cent in 3.7 minutes and 95 per cent in 10 minutes.

In using the oral route for determination of the hydrochloric acid secretion in the stomach without the gastric tube, one must be careful that the patient has not received substances containing aluminum, bismuth, barium, calcium, magnesium, kaolin, iron or vitamins for at least 48 hours prior to the administration of Diagnex (new formula). An elevated concentration of urea in the blood does not seem to interfere with the ability to secrete quinine, nor does albuminuria interfere with the test for quinine. The azure, a cation, is released from the compound if hydrochloric acid is present and is detected by the change of color in the urine.

Lack of space prevents further elaboration on the many useful suggestions found throughout the Annual Review of Medicine but it is recommended that all physicians who are interested in medical progress, add this volume to their library.

THERAPY OF FUNGUS DISEASES: Thomas H. Sternberg, M.D., Professor of Medicine (Dermatology) and Assistant Dean for Postgraduate Medical Education, and Victor D. Newcomer, M.D., Associate Professor of Medicine (Dermatology), University of California School of Medicine, Los Angeles, Calif. 337 pages, illustrated. Little, Brown & Co., Boston, Mass., 1955. Price $7.50.

The numerous contributions to "Therapy of Fungus Diseases" are a comprehensive review and summary of fungus infections and therapy. Inorganic, organic and antibiotic preparations, their value and effect on fungi is an interesting study. Physicians in general practice, dermatologists and others who come in contact with fungus diseases will greatly benefit by reading this excellent treatise.

CIBA FOUNDATION SYMPOSIUM ON EXPERIMENTAL TUBERCULOSIS, BACILLUS AND HOST WITH AN ADDENDUM ON LEPROSY: Editors for the Ciba Foundation—G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Margaret P. Cameron, M.A., B.A.L.S.—Assisted by: Cecilia M. O'Connor, B.Sc. 396 pages, 69 illustrations. Little Brown & Co., Boston, Mass., 1955. Price $9.00.

A highly scientific book on tuberculosis and leprosy, the outcome of a symposium on "The Tubercle Bacillus and the Reactions of the Host Tissues", held on 5-7 October 1954. Research workers, clinicians and others interested in tuberculosis and leprosy contributed to this highly specialized volume.

Readers are presented with the ultimate in these diseases and their effect on human beings. Physicians, public health workers and laboratory researchers will find many useful suggestions and theories embodied between the covers.

CURRENT THERAPY 1956: Edited by Howard I. Conn, M.D., with several well known co-editors. 632 pages. W. B. Saunders Co., Philadelphia, Pa., 1956. Price $11.00.

This edition of "Current Therapy", with contributors well known in their specialty, has brought to the medical profession a volume in which the busy physician will find answers to many of his puzzling problems in medicine.

Should the physician be interested in infectious diseases, he will find up to date and detailed description of the latest and improved treatment of the given condition. For example, poliomyelitis: Dr. Jessie Wright of the University of Pittsburgh describes the preparation for vaccination of the patient, the time between administration of the second dose of the vaccine and when the third or booster dose is to begin (7 to 10 months after the second inoculation). The Salk vaccine contains material from all three types of virus, therefore, the vaccine is called trivalent.

A comprehensive and detailed description is also given for the treatment of the various complications which may occur in a given patient. Page 57 is especially applicable to general practitioners and pediatricians. It deals with schedules for active

immunization to the common infectious diseases.

Other disease groups are also taken up in detail and should be carefully read.

Section 5, "Diseases of the Digestive System", under the editorship of Dr. Walter L. Palmer, President of the American College of Physicians, and co-authors, is up to date and contains many nuggets which will aid the doctor in daily office or hospital work.

All in all, the entire volume is well prepared, easy reading and can be recommended to all physicians.

PRACTICAL GASTROENTEROLOGY: Ernst Hafter, M.D., with contributions by H. Hotz, M.D. and F. Deucher, M.D., Zurich and Luzern. 380 pages, 148 illustrations. Georg Thieme Verlag, Stuttgart, 1956. Price $11.40.

The progress in gastroenterology has become so great during the last years, that the nonspecialist is unable to follow all new developments. Hafter has written this book in cooperation with Hotz and Deucher with the intention of presenting to all those interested, the newest findings in this field. In order to make his colleagues cognizant of the work being done in other countries, he cites and refers to publications that are not so well known in Europe. As he has limited his book to a practical size, it is natural that not all authors could be cited. Of course, radiology plays an important part in this book. The illustrations are very instructive, though not complete. But all conditions, which are very frequently seen in the general practice, are illustrated and thoroughly discussed. Besides the diagnostic sections; medical, surgical and dietary therapy are thoroughly discussed. The publication gives many valuable clinical suggestions, which will interest all readers. The illustrations are excellent and we want to compliment Thieme publishers, on their high standard of publications. We can recommend this book to all those who are interested in gastroenterology; that means, practitioners, students, surgeons, internists and gastroenterologists. They will find valuable advice in this field.

Most interesting are the early cases of carcinoma of the stomach, cases of gastritis and functional conditions of the stomach and intestine. For the American physician it will be interesting to compare the therapeutics and dietary notes with the experiences gained in this country.

PATHOLOGIA DEL ESTOMAGO OPERADO: Secundo Congress Argentina de Gastroenterologia—13-18 April 1953. 481 pages, illustrated. Editorial Universitaria, Buenos Aires, Arg.

The contents of this treatise represent the papers presented at the Second Congress of Gastroenterology, Argentina, in cooperation with the radiological and medical organizations.

The ten chapters represent the latest in the science of digestive diseases with special reference to the operated stomach. The contributors are outstanding clinicians in their respective specialties.

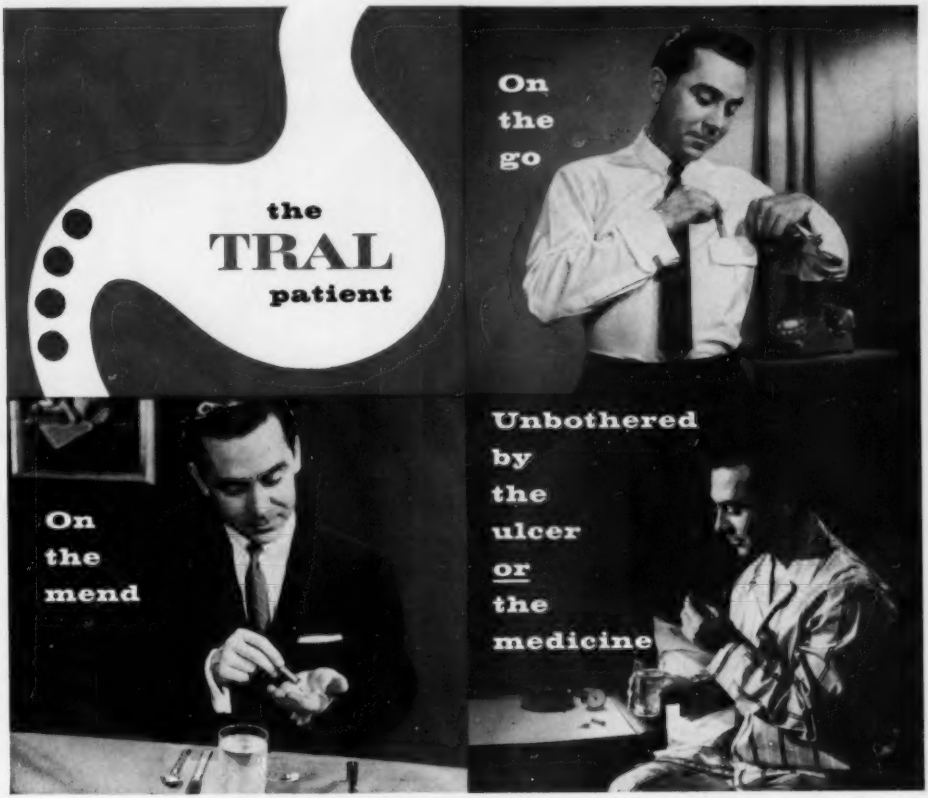
Unfortunately, the black and white roentgen studies are rather poor. However, the explanations are adequate, the type and format are well done.

ELECTROCARDIOGRAPHIC TEST BOOK—VOL. 1 AND 2: Travis Winsor, Editor, with an array of advisory and review panel. 299 pages, illustrated. The American Heart Association, Inc., New York, N. Y., 1956. Price $5.00 per set.

These two volumes issued by the Committee on Professional Education of the American Heart Association, Inc., should be in the hands of all medical students and all physicians. They are easily read, understood and simplify the diagnosis of normal and abnormal involvement of the heart.

The graphs and roentgen illustrations and accompanying explanations are clear and concise, so that even the novice will find little difficulty in understanding the pathology.

These two volumes can be highly recommended.



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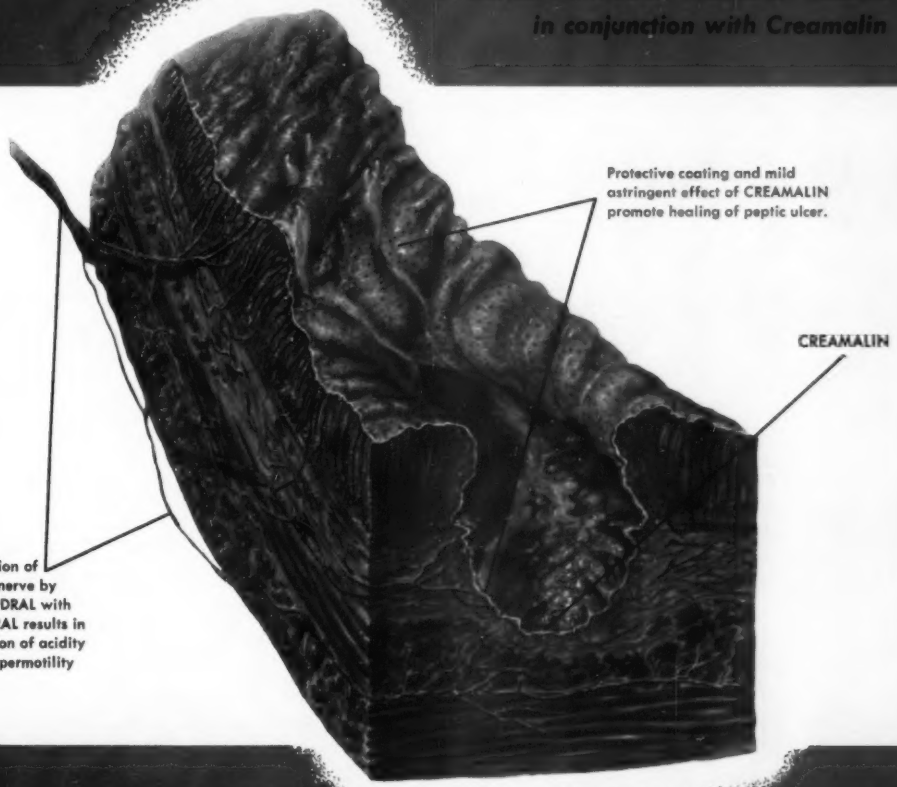

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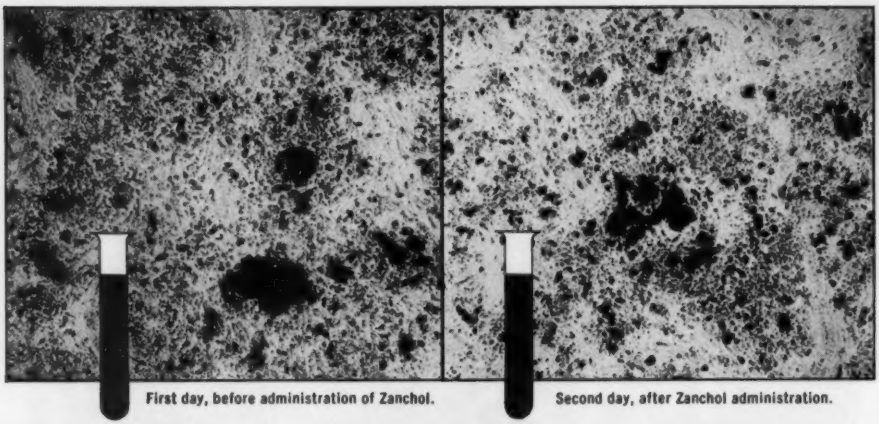
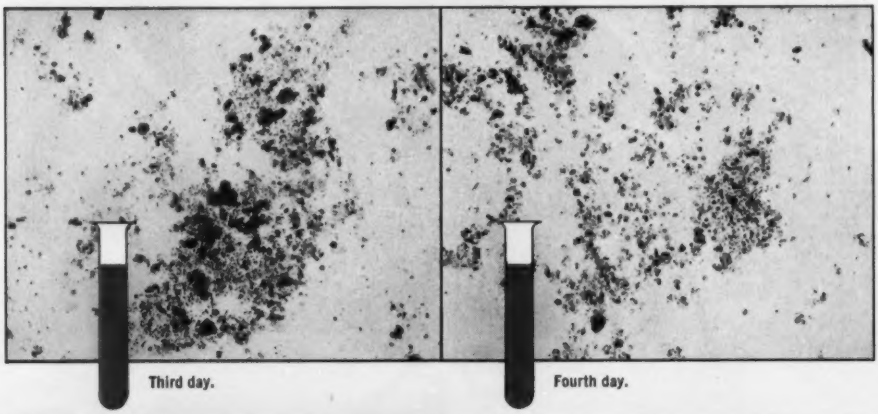


First day, before administration of Zanchol.

Second day, after Zanchol administration.

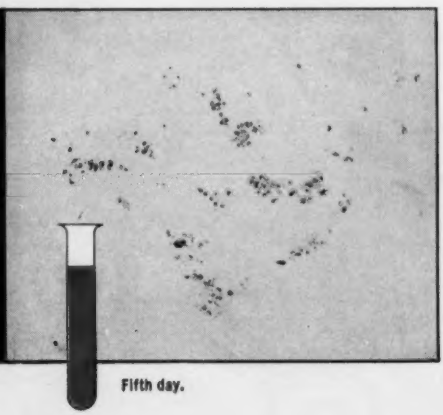


Third day.

Fourth day.

photomicrographs[1]

showing daily changes in sediment from centrifuged bile taken from T-tube drainage in a postcholecystectomized patient.



Fifth day.

Effective bacteriostasis in bowel surgery

SULFATHALIDINE®

PHTHALYLSULFATHIAZOLE

SULFATHALIDINE, used before and after surgery, rapidly suppresses intestinal pathogens, particularly coliforms. This virtual "sterilization" of the G. I. tract minimizes the hazard of peritonitis and secondary infection.

With SULFATHALIDINE, the stool is soft (not fluid), flatus is minimal...tissue repair is thereby enhanced.

Absorption of SULFATHALIDINE is very low—bacteriostatic performance is concentrated where desired—in the gut.

Also supplied as palatable CREMOTHALIDINE® Suspension, each teaspoonful containing 1.0 Gm. of SULFATHALIDINE.

MSD

MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.


more CERTAIN
CONTROL OF DIARRHEA
(whether toxic, neuromuscular or emotional in origin)
because
more COMPREHENSIVE in therapeutic effects
• adsorbs toxins
• soothes mucosa
• reduces hyperperistalsis
• neutralizes hyperacidity
• eases emotional tension
DONNAGEL®
Robins
(DONNATAL WITH KAOLIN AND PECTIN COMPOUND)
Each 30 cc. of Donnagel contains:
Hyoscyamine Sulfate ..... 0.1037 mg.
Atropine Sulfate ..... 0.0194 mg.
Hyoscine Hydrobromide.. 0.0065 mg.
Phenobarbital (¼ gr.)..... 16.2 mg.
Kaolin (90 gr.)..... 6.0 Gm.
Pectin (2 gr.).....130.0 mg.
Dihydroxy aluminum aminoacetate (7½ gr.).. 0.5 Gm.
Robins
A. H. ROBINS CO., INC., RICHMOND 20, VA.
Ethical Pharmaceuticals of Merit since 1878

" . . . Well, I always prescribe Rorer's Maalox. It's an excellent antacid, doesn't constipate and patients will take it indefinitely."

. . . . . .

MAALOX® suspension, bottles of 12 fluidounces *(sample on request)*; tablets, bottles of 100.

An efficient antacid suspension of magnesium-aluminum hydroxide gel; tablets, 0.4 Gm.

WILLIAM H. RORER, INC. 4865 Stenton Ave., Philadelphia 44, Pennsylvania

"...an ideal treatment for the diarrheal syndrome..."[1]

RESION

(POLYAMINE METHYLENE RESIN AND SYNTHETIC SILICATES)

faster relief[1]

In 90 patients treated with Resion, 86 (95%) were controlled in 8 to 12 hours, even faster than with bismuth and paregoric.

twice as effective[2]

THERAPY	% SUCCESSES
RESION	**92**
Kaolin and Pectin	40
Bismuth and Paregoric	50

safe[3]*...and non-constipating*[1-3]

The multiple adsorbent and ion-exchange materials in Resion are "totally insoluble and non-toxic."[3] No cases of constipation reported in three clinical series of more than 250 patients.[1-3]

Available IN 2 PLEASANT-TASTING DOSAGE FORMS

Resion—for simple diarrhea. Polyamine methylene resin 10%; Sodium aluminum silicate (synthetic) 10%; Magnesium aluminum silicate (synthetic) 1.25%.

Resion P-M-S—for infectious diarrhea. Resion; plus Polymyxin-B 125,000 units; Phthalylsulfacetamide 1.0 Gm.; Methyl Paraben 1.33%; Propyl Paraben 0.33%; Butyl Paraben 0.1%; in each tablespoonful (15 ml.)

Dosage: *RESION*.....1 tablespoonful hourly for 4 doses; then every three hours while awake.

RESION P-M-S....1 tablespoonful hourly for 3 doses; then 3 times daily. Infants—the same schedule as above, but in teaspoonful doses.

Supplied: Resion is supplied in bottles of 4 and 12 fluid ounces; Resion P-M-S in bottles of 4 fluid ounces.

REFERENCES: 1. Weiss, J.: K.A.G.P. Journal 2:33, 1956. 2. Gabroy, H. K., and Selsman, G. J. V.: Amer. J. Dig. Dis. 20:395, 1953. 3. Lichtman, A. L.: Exper. Med. & Surg. 9:90, 1951.

Products of Original Research

NATIONAL

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in frequency of incidence . . .
"The symptom complex of nausea and vomiting is second only to pain as a clinical manifestation of disease."[1]

BONAMINE*

BRAND OF MECLIZINE HYDROCHLORIDE

provides long-lasting control of the nausea, vomiting, and vertigo:

IN DRUG-INDUCED EMESIS Bonamine depresses vestibular sensitivity, accounting in part for its "effectiveness in alleviating opiate-induced vomiting . . . [and] in combating vestibular vertigo and the toxic vestibular effects of streptomycin."[1]

IN EMESIS SECONDARY TO INFECTIONS AND TOXICOSES Bonamine is "successful in controlling the vomiting associated with common pediatric infections and toxicoses."[1] Side effects such as drowsiness are "infrequent."[1]

IN POSTOPERATIVE VOMITING "Bonamine is a suppressor of postoperative nausea and vomiting, and has a potential use in contributing to the . . . clinical well-being of patients recovering from surgery requiring general anesthesia."[2]

IN VERTIGO DUE TO CEREBRAL ARTERIOSCLEROSIS Bonamine affords a high degree of relief of vertigo in patients with cerebral manifestations. "The lack of adverse effects . . . suggests that long-term use of this drug . . . is a reasonable procedure in the management of such patients."[3]

IN MOTION SICKNESS In any kind of travel, Bonamine is the only motion-sickness preventive effective in a single daily dose; notably safe and free of side effects.[4]

Bonamine is also valuable in treating the dizziness and emesis associated with radiation therapy, Ménière's syndrome, fenestration procedures, and labyrinthitis.

Available as scored, tasteless tablets, 25 mg.; and as mint-flavored chewing tablets, 25 mg.

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2. Kinney, J. J.: J. M. Soc. New Jersey *53*:128 (March) 1956.
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*Trademark

PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N. Y. Pfizer

for abnormal bowel function use

L. A.® Formula

It is important, when inducing normal bowel function, to supply a non-irritating bulk to the colon, especially in those cases in which it has been necessary to eliminate from the diet the high roughage foods containing irritating bulk (lignin and cellulose).

It has been shown[1] that the colon resumes a more normal peristaltic pattern[2] when it is supplied with a stool of medium soft consistency of sufficient bulk[3], especially if the indigestible portion of that bulk consists primarily of hemicellulose[4].

L. A. FORMULA is a vegetable concentrate of naturally occurring hemicelluloses. It is derived from blond psyllium seed by our special Ultra-Pulverization Process and simultaneously dispersed in lactose and dextrose. It provides just the moist, smooth, effective[5] bulk so essential to normal peristalsis.

Furthermore, L. A. FORMULA is undetectable in fruit juice and milk, pleasant tasting in water, and available in 7 and 14 ounce containers at significantly lower cost-to-patient prices. That's why we say L. A. FORMULA

... to normalize

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Formula: 50% plantago ovata coating dispersed in lactose and dextrose.

Made by BURTON, PARSONS & COMPANY *Since 1939*

Originators of Fine Hydrophilic Colloids

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when he smokes too much . . .

Whenever indigestion results from habitual overdoing in any form (excess of cigarettes or alcohol, dietary indiscretion, nervous tension), symptoms can be quickly alleviated night and day with Gelusil and the new formulation Gelusil-Lac.

To avoid daytime distress: Gelusil provides the sustained action of magnesium trisilicate and specially prepared aluminum hydroxide gel to restore and maintain gastric pH within normal range. Because it does not overneutralize or alkalize, Gelusil avoids the twin dangers of acid rebound and systemic alkalosis.

To prevent middle-of-the-night attacks: In Gelusil-Lac, the proven antacid action of Gelusil is combined with sustained buffering effect of specially prepared high protein (low fat) milk solids to prevent gastric pain at night.

Nonconstipating: The specially prepared aluminum hydroxide component in Gelusil has a low order of chemical activity. Thus formation of astringent – and constipating – aluminum chloride is minimal.

Dosage: 2 Gelusil tablets or 2 teaspoonfuls Gelusil liquid two hours after eating or when symptoms are pronounced. Each tablet or teaspoonful provides: 7½ gr. magnesium trisilicate and 4 gr. aluminum hydroxide gel. Gelusil-Lac: At bedtime, one heaping tablespoonful stirred rapidly into one-half glass (4 fl. oz.) of cool water. (Provides equivalent of 4 Gelusil tablets.)

Gelusil®/Gelusil-Lac

WARNER-CHILCOTT

100 YEARS OF SERVICE TO THE MEDICAL PROFESSION